STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 212900

TO: Ralph J Gitomer
Location: rem/3D65/3C70
Art Unit: 1657
Tuesday, January 23, 2007
Case Serial Number: 10/701990

From: Derrick Blalock
Location: Biotech-Chem Library
REM-1A62
Phone: (571)272-1120

derrick.blalock@uspto.gov

Search Notes

Examiner Gitomer,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Derrick Blalock
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-1120

Search History

```
                ACT GIT990BI1AU/A
                ---------
L1   (       228)SEA ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L2   (       139)SEA ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L3             8 SEA ABB=ON  PLU=ON  L1 AND L2
                ---------

     FILE 'EMBASE' ENTERED AT 14:07:44 ON 23 JAN 2007
                ACT GIT990EM1AU/A
                ---------
L4   (         4)SEA ABB=ON  PLU=ON  (10390-17-7/BI OR 18991-62-3/BI OR
                 50-99-7/BI OR 66034-51-3/BI)
L5   (       134)SEA ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L6   (        62)SEA ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L7               SEL PLU=ON  L4 1- NAME :      41 TERMS
L8   (    251111)SEA ABB=ON  PLU=ON  L7
L9   (    251111)SEA ABB=ON  PLU=ON  L8 OR L4
L10  (    704774)SEA ABB=ON  PLU=ON  BODY FLUID+NT/CT
L11  (      9901)SEA ABB=ON  PLU=ON  GLYCOLYSIS+NT/CT
L12  (     78151)SEA ABB=ON  PLU=ON  OBESITY+NT/CT
L13  (         4)SEA ABB=ON  PLU=ON  L5 AND L6
L14  (        48)SEA ABB=ON  PLU=ON  L5 AND L9
L15  (         0)SEA ABB=ON  PLU=ON  L14 AND L11
L16  (         4)SEA ABB=ON  PLU=ON  L14 AND L12
L17  (    215419)SEA ABB=ON  PLU=ON  FATTY ACID+NT/CT
L18  (        28)SEA ABB=ON  PLU=ON  L5 AND L17
L19  (         0)SEA ABB=ON  PLU=ON  L18 AND  L11
L20  (         2)SEA ABB=ON  PLU=ON  L18 AND  L10
L21            9 SEA ABB=ON  PLU=ON  (L13 OR L15 OR L16 OR L19 OR L20)
                ---------

     FILE 'HCAPLUS' ENTERED AT 14:07:46 ON 23 JAN 2007
                ACT GIT990HC1AU/A
                ---------
L22  (         4)SEA ABB=ON  PLU=ON  (10390-17-7/BI OR 18991-62-3/BI OR
                 50-99-7/BI OR 66034-51-3/BI)
L23  (    198890)SEA ABB=ON  PLU=ON  L22
L24  (   1000951)SEA ABB=ON  PLU=ON  BODY FLUID+OLD,NT/CT
L25  (     14923)SEA ABB=ON  PLU=ON  GLYCOLYSIS+OLD/CT
L26  (     29547)SEA ABB=ON  PLU=ON  OBESITY+NT/CT
L27  (       136)SEA ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L28  (        30)SEA ABB=ON  PLU=ON  L27 AND L23
L29  (         2)SEA ABB=ON  PLU=ON  L28 AND L25
L30  (         4)SEA ABB=ON  PLU=ON  L28 AND L26
L31  (        13)SEA ABB=ON  PLU=ON  L28 AND L24
L32           15 SEA ABB=ON  PLU=ON  (L29 OR L30 OR L31)
                ---------

     FILE 'MEDLINE' ENTERED AT 14:07:48 ON 23 JAN 2007
                ACT GIT990MD1AU/A
                ---------
L33  (       128)SEA ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L34  (        59)SEA ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L35  (         4)SEA ABB=ON  PLU=ON  L33 AND L34
L36  (     21152)SEA ABB=ON  PLU=ON  INSULIN RESISTANCE+NT/CT
L37  (         2)SEA ABB=ON  PLU=ON  L33 AND L36
L38            6 SEA ABB=ON  PLU=ON  (L35 OR L37)
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     FILE 'WPIX' ENTERED AT 14:07:50 ON 23 JAN 2007
                ACT GIT990WX1AU/A
                ---------
L39 (        26)SEA ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L40 (     13935)SEA ABB=ON  PLU=ON  OBESITY/BI,ABEX OR OBESE/BI,ABEX
L41           4 SEA ABB=ON  PLU=ON  L39 AND L40
                ---------

     FILE 'BIOSIS' ENTERED AT 14:08:14 ON 23 JAN 2007
                ACT GIT990BI1A/A
                ---------
L42 (       139)SEA ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L43 (   3051894)SEA ABB=ON  PLU=ON  BODY FLUID OR BLOOD OR TEAR OR URINE OR
                BLOOD OR PLASMA OR SALIVA OR SWEAT
L44 (     82233)SEA ABB=ON  PLU=ON  OBESITY OR OBESE
L45 (     15922)SEA ABB=ON  PLU=ON  GLYCOLYSIS OR EMBDEN MEYERHOF
L46 (        64)SEA ABB=ON  PLU=ON  L42 AND L43
L47 (         2)SEA ABB=ON  PLU=ON  L44 AND L46
L48 (         1)SEA ABB=ON  PLU=ON  L46 AND L45
L49 (         6)SEA ABB=ON  PLU=ON  L42 AND L45
L50 (        10)SEA ABB=ON  PLU=ON  L42(15A)L43
L51          17 SEA ABB=ON  PLU=ON  (L47 OR L48 OR L49 OR L50)
                ---------

     FILE 'EMBASE' ENTERED AT 14:08:16 ON 23 JAN 2007
                ACT GIT990EM1A/A
                ---------
L52 (         4)SEA ABB=ON  PLU=ON  (10390-17-7/BI OR 18991-62-3/BI OR
                50-99-7/BI OR 66034-51-3/BI)
L53 (        62)SEA ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L54             SEL PLU=ON  L52 1- NAME :      41 TERMS
L55 (    251111)SEA ABB=ON  PLU=ON  L54
L56 (    251111)SEA ABB=ON  PLU=ON  L55 OR L52
L57 (    704774)SEA ABB=ON  PLU=ON  BODY FLUID+NT/CT
L58 (      9901)SEA ABB=ON  PLU=ON  GLYCOLYSIS+NT/CT
L59 (     78151)SEA ABB=ON  PLU=ON  OBESITY+NT/CT
L60 (     24230)SEA ABB=ON  PLU=ON  INSULIN RESISTANCE/CT
L61 (         2)SEA ABB=ON  PLU=ON  L53 AND L60
L62 (         2)SEA ABB=ON  PLU=ON  L53 AND L59
L63 (         5)SEA ABB=ON  PLU=ON  L53 AND L58
L64 (        11)SEA ABB=ON  PLU=ON  L53 AND L57
L65 (        18)SEA ABB=ON  PLU=ON  (L61 OR L62 OR L63 OR L64)
L66 (      4833)SEA ABB=ON  PLU=ON  L56 AND L58
L67 (       132)SEA ABB=ON  PLU=ON  L66 AND L60
L68 (   1276689)SEA ABB=ON  PLU=ON  DRUG ADMINISTRATION ROUTE+NT/CT
L69 (        18)SEA ABB=ON  PLU=ON  L67 AND L68
L70          29 SEA ABB=ON  PLU=ON  (L65 OR L69) AND PY<=2003
                ---------

     FILE 'HCAPLUS' ENTERED AT 14:08:19 ON 23 JAN 2007
                ACT GIT990HC1A/A
                ---------
L71 (         4)SEA ABB=ON  PLU=ON  (10390-17-7/BI OR 18991-62-3/BI OR
                50-99-7/BI OR 66034-51-3/BI)
L72 (    198890)SEA ABB=ON  PLU=ON  L71
L73 (        58)SEA ABB=ON  PLU=ON  DEUTER?/OBI(A)GLUCOSE/OBI
L74 (   1000951)SEA ABB=ON  PLU=ON  BODY FLUID+OLD,NT/CT
L75 (         9)SEA ABB=ON  PLU=ON  L73 AND L74
L76 (         0)SEA ABB=ON  PLU=ON  L73 AND INSULIN+OLD,NT/CT
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L77 (      14923)SEA ABB=ON  PLU=ON  GLYCOLYSIS+OLD/CT
L78 (          1)SEA ABB=ON  PLU=ON  L73 AND L77
L79 (      18294)SEA ABB=ON  PLU=ON  TEST KITS/CT
L80 (          1)SEA ABB=ON  PLU=ON  L73 AND L79
L81 (          0)SEA ABB=ON  PLU=ON  L73 AND INSULIN/OBI
L82 (       8650)SEA ABB=ON  PLU=ON  HIGH THROUGHPUT SCREENING/CT
L83 (          3)SEA ABB=ON  PLU=ON  L73 AND PATENT/DT
L84 (         55)SEA ABB=ON  PLU=ON  L73 NOT L83
L85 (         52)SEA ABB=ON  PLU=ON  L84 AND PY<=2003
L86 (          0)SEA ABB=ON  PLU=ON  L85 AND L77
L87 (          6)SEA ABB=ON  PLU=ON  L85 AND L74
L88 (          0)SEA ABB=ON  PLU=ON  L85 AND L79
L89 (       3942)SEA ABB=ON  PLU=ON  L72 AND L77
L90 (          1)SEA ABB=ON  PLU=ON  L89 AND L82
L91 (          9)SEA ABB=ON  PLU=ON  L89 AND L79
L92 (      29547)SEA ABB=ON  PLU=ON  OBESITY+NT/CT
L93 (          0)SEA ABB=ON  PLU=ON  L85 AND L92
L94           17 SEA ABB=ON  PLU=ON  (L75 OR L76 OR L78 OR L80 OR L81 OR L86 OR
                 L87 OR L88 OR L90 OR L91 OR L93)
               ---------

     FILE 'MEDLINE' ENTERED AT 14:08:21 ON 23 JAN 2007
                 ACT GIT990MD1A/A
                 ---------
L95 (          4)SEA ABB=ON  PLU=ON  (10390-17-7/BI OR 18991-62-3/BI OR
                 50-99-7/BI OR 66034-51-3/BI)
L96               SEL PLU=ON  L95 1- NAME :      41 TERMS
L97 (     295569)SEA ABB=ON  PLU=ON  L96
L98 (     295569)SEA ABB=ON  PLU=ON  L97 OR L95
L99 (         59)SEA ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L100(    1992458)SEA FILE=MEDLINE ABB=ON  PLU=ON  BODY FLUIDS+NT/CT
L101(      21152)SEA FILE=MEDLINE ABB=ON  PLU=ON  INSULIN RESISTANCE+NT/CT
L102(         28)SEA FILE=MEDLINE ABB=ON  PLU=ON  L99 AND L100
L103(          2)SEA FILE=MEDLINE ABB=ON  PLU=ON  L102 AND L101
L104(          3)SEA FILE=MEDLINE ABB=ON  PLU=ON  L99 AND L101
L105(      12366)SEA FILE=MEDLINE ABB=ON  PLU=ON  GLYCOLYSIS/CT
L106(          6)SEA FILE=MEDLINE ABB=ON  PLU=ON  L99 AND L105
L107(      12470)SEA FILE=MEDLINE ABB=ON  PLU=ON  L98 AND L101
L108(       7044)SEA FILE=MEDLINE ABB=ON  PLU=ON  L107 AND L100
L109(         36)SEA FILE=MEDLINE ABB=ON  PLU=ON  L108 AND L105
L110(      73584)SEA FILE=MEDLINE ABB=ON  PLU=ON  OBESITY+NT/CT
L111(         10)SEA FILE=MEDLINE ABB=ON  PLU=ON  L109 AND L110
L112(         19)SEA FILE=MEDLINE ABB=ON  PLU=ON  (L103 OR L104 OR L106 OR L111)
L113(         14)SEA FILE=MEDLINE ABB=ON  PLU=ON  L112 AND PY<=2003
L114(     390158)SEA FILE=MEDLINE ABB=ON  PLU=ON  FATTY ACIDS+NT/CT
L115(         12)SEA FILE=MEDLINE ABB=ON  PLU=ON  L114 AND L100 AND L101 AND L10
L116(         12)SEA FILE=MEDLINE ABB=ON  PLU=ON  L115 AND PY<=2003
L117          23 SEA ABB=ON  PLU=ON  L113 OR L116
               ---------

     FILE 'WPIX' ENTERED AT 14:08:23 ON 23 JAN 2007
                 ACT GIT990WX1A/A
                 ---------
L118           7 SEA ABB=ON  PLU=ON  DEUTER?/BI,ABEX(5A)GLUCOSE/BI,ABEX
                 ---------

     FILE 'BIOSIS' ENTERED AT 14:11:07 ON 23 JAN 2007
                 D QUE L3

     FILE 'EMBASE' ENTERED AT 14:12:21 ON 23 JAN 2007
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            D QUE L21

     FILE 'HCAPLUS' ENTERED AT 14:12:30 ON 23 JAN 2007
            D QUE L32

     FILE 'MEDLINE' ENTERED AT 14:12:40 ON 23 JAN 2007
            D QUE L38

     FILE 'WPIX' ENTERED AT 14:12:48 ON 23 JAN 2007
            D QUE L41

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, HCAPLUS' ENTERED AT 14:13:14 ON 23
     JAN 2007
L119         30 DUP REM L38 L3 L21 L41 L32 (12 DUPLICATES REMOVED)

     FILE 'BIOSIS' ENTERED AT 14:14:14 ON 23 JAN 2007
            D QUE L51
L120         17 SEA ABB=ON  PLU=ON  L51 NOT L3

     FILE 'EMBASE' ENTERED AT 14:14:30 ON 23 JAN 2007
            D QUE L70
L121         26 SEA ABB=ON  PLU=ON  L70 NOT L21

     FILE 'HCAPLUS' ENTERED AT 14:15:28 ON 23 JAN 2007
            D QUE L94
L122         14 SEA ABB=ON  PLU=ON  L94 NOT L32

     FILE 'MEDLINE' ENTERED AT 14:15:45 ON 23 JAN 2007
            D QUE L117
L123         23 SEA ABB=ON  PLU=ON  L117 NOT L38

     FILE 'WPIX' ENTERED AT 14:16:20 ON 23 JAN 2007
            D QUE L118
L124          7 SEA ABB=ON  PLU=ON  L118 NOT L41

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, HCAPLUS' ENTERED AT 14:16:52 ON 23
     JAN 2007
L125         76 DUP REM L123 L120 L121 L124 L122 (11 DUPLICATES REMOVED)

=>
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Author Search

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=> FILE BIOSIS
FILE 'BIOSIS' ENTERED AT 14:11:07 ON 23 JAN 2007
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 17 January 2007 (20070117/ED)


=> D QUE L3
L1   (       228)SEA FILE=BIOSIS ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L2   (       139)SEA FILE=BIOSIS ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L3             8 SEA FILE=BIOSIS ABB=ON  PLU=ON  L1 AND L2


=> file EMBASE
FILE 'EMBASE' ENTERED AT 14:12:21 ON 23 JAN 2007
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 FILE COVERS 1974 TO 23 Jan 2007 (20070123/ED)

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> D QUE L21
L4   (         4)SEA FILE=REGISTRY ABB=ON  PLU=ON  (10390-17-7/BI OR 18991-62-3/
                 BI OR 50-99-7/BI OR 66034-51-3/BI)
L5   (       134)SEA FILE=EMBASE ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L6   (        62)SEA FILE=EMBASE ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L7               SEL  PLU=ON  L4 1- NAME :      41 TERMS
L8   (    251111)SEA FILE=EMBASE ABB=ON  PLU=ON  L7
L9   (    251111)SEA FILE=EMBASE ABB=ON  PLU=ON  L8 OR L4
L10  (    704774)SEA FILE=EMBASE ABB=ON  PLU=ON  BODY FLUID+NT/CT
L11  (      9901)SEA FILE=EMBASE ABB=ON  PLU=ON  GLYCOLYSIS+NT/CT
L12  (     78151)SEA FILE=EMBASE ABB=ON  PLU=ON  OBESITY+NT/CT
L13  (         4)SEA FILE=EMBASE ABB=ON  PLU=ON  L5 AND L6
L14  (        48)SEA FILE=EMBASE ABB=ON  PLU=ON  L5 AND L9
L15  (         0)SEA FILE=EMBASE ABB=ON  PLU=ON  L14 AND L11
L16  (         4)SEA FILE=EMBASE ABB=ON  PLU=ON  L14 AND L12
L17  (    215419)SEA FILE=EMBASE ABB=ON  PLU=ON  FATTY ACID+NT/CT
L18  (        28)SEA FILE=EMBASE ABB=ON  PLU=ON  L5 AND L17
L19  (         0)SEA FILE=EMBASE ABB=ON  PLU=ON  L18 AND  L11
L20  (         2)SEA FILE=EMBASE ABB=ON  PLU=ON  L18 AND  L10
L21            9 SEA FILE=EMBASE ABB=ON  PLU=ON  (L13 OR L15 OR L16 OR L19 OR
                 L20)


=> FILE HCAPLUS
FILE 'HCAPLUS' ENTERED AT 14:12:30 ON 23 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 23 Jan 2007 VOL 146 ISS 5
FILE LAST UPDATED: 22 Jan 2007 (20070122/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> D QUE L32
L22 (4)SEA FILE=REGISTRY ABB=ON PLU=ON (10390-17-7/BI OR 18991-62-3/
BI OR 50-99-7/BI OR 66034-51-3/BI)
L23 (198890)SEA FILE=HCAPLUS ABB=ON PLU=ON L22
L24 (1000951)SEA FILE=HCAPLUS ABB=ON PLU=ON BODY FLUID+OLD,NT/CT
L25 (14923)SEA FILE=HCAPLUS ABB=ON PLU=ON GLYCOLYSIS+OLD/CT
L26 (29547)SEA FILE=HCAPLUS ABB=ON PLU=ON OBESITY+NT/CT
L27 (136)SEA FILE=HCAPLUS ABB=ON PLU=ON HELLERSTEIN M?/AU
L28 (30)SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L23
L29 (2)SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND L25
L30 (4)SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND L26
L31 (13)SEA FILE=HCAPLUS ABB=ON PLU=ON L28 AND L24
L32 15 SEA FILE=HCAPLUS ABB=ON PLU=ON (L29 OR L30 OR L31)

=> FILE MEDLINE
FILE 'MEDLINE' ENTERED AT 14:12:40 ON 23 JAN 2007

FILE LAST UPDATED: 20 Jan 2007 (20070120/UP). FILE COVERS 1950 TO DATE.

All regular MEDLINE updates from November 15 to December 16 have been
added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R))
and 2007 tree numbers.

The annual reload will be available in early 2007.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> D QUE L38
L33 (128)SEA FILE=MEDLINE ABB=ON PLU=ON HELLERSTEIN M?/AU
L34 (59)SEA FILE=MEDLINE ABB=ON PLU=ON DEUTER?(2A)GLUCOSE
L35 (4)SEA FILE=MEDLINE ABB=ON PLU=ON L33 AND L34
L36 (21152)SEA FILE=MEDLINE ABB=ON PLU=ON INSULIN RESISTANCE+NT/CT
L37 (2)SEA FILE=MEDLINE ABB=ON PLU=ON L33 AND L36
L38 6 SEA FILE=MEDLINE ABB=ON PLU=ON (L35 OR L37)

=> FILE WPIX
FILE 'WPIX' ENTERED AT 14:12:48 ON 23 JAN 2007
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FILE LAST UPDATED:                          19 JAN 2007   <20070119/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE:      200705        <200705/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> YOU ARE IN THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX <<<

>>> IPC Reform reclassification data for the backfile is being
    loaded into the database during January 2007.
    There will not be any update date (UP) written for the reclassified
    documents, but they can be identified by 20060101/UPIC. <<<

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf


>>> FOR DETAILS ON THE NEW AND ENHANCED DERWENT WORLD PATENTS INDEX
    PLEASE SEE
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

>>> New and revised Manual Codes went live in Derwent World Patents Index
    To view the lists of new, revised and retired codes for both CPI and
    EPI,  please go to:
    http://scientific.thomson.com/dwpi-manualcoderevision <<<
'BI,ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> D QUE L41
L39 (        26)SEA FILE=WPIX ABB=ON  PLU=ON  HELLERSTEIN M?/AU
L40 (     13935)SEA FILE=WPIX ABB=ON  PLU=ON  OBESITY/BI,ABEX OR OBESE/BI,ABEX

L41            4 SEA FILE=WPIX ABB=ON  PLU=ON  L39 AND L40


=> DUP REM L38 L3 L21 L41 L32
FILE 'MEDLINE' ENTERED AT 14:13:14 ON 23 JAN 2007

FILE 'BIOSIS' ENTERED AT 14:13:14 ON 23 JAN 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 14:13:14 ON 23 JAN 2007
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FILE 'HCAPLUS' ENTERED AT 14:13:14 ON 23 JAN 2007
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PROCESSING COMPLETED FOR L38
PROCESSING COMPLETED FOR L3
PROCESSING COMPLETED FOR L21
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PROCESSING COMPLETED FOR L41
PROCESSING COMPLETED FOR L32
L119          30 DUP REM L38 L3 L21 L41 L32 (12 DUPLICATES REMOVED)
                 ANSWERS '1-6' FROM FILE MEDLINE
                 ANSWERS '7-10' FROM FILE BIOSIS
                 ANSWERS '11-16' FROM FILE EMBASE
                 ANSWERS '17-20' FROM FILE WPIX
                 ANSWERS '21-30' FROM FILE HCAPLUS

=> D IALL 1-16;D IALL ABEQ TECH 17-20;D IBIB ED ABS 21-30

L119 ANSWER 1 OF 30     MEDLINE on STN                    DUPLICATE 3
ACCESSION NUMBER:   2002080950     MEDLINE  Full-text
DOCUMENT NUMBER:    PubMed ID: 11807713
TITLE:              CD4+ T cell kinetics and activation in human
                    immunodeficiency virus-infected patients who remain viremic
                    despite long-term treatment with protease inhibitor-based
                    therapy.
AUTHOR:             Deeks Steven G; Hoh Rebecca; Grant Robert M; Wrin Terri;
                    Barbour Jason D; Narvaez Amy; Cesar Denise; Abe Ken; Hanley
                    Mary Beth; Hellmann Nicholas S; Petropoulos Christos J;
                    McCune Joseph M; Hellerstein Marc K
CORPORATE SOURCE:   Department of Medicine, University of California at San
                    Francisco and San Francisco General Hospital, San
                    Francisco, CA 94110, USA.. sdeeks@php.ucsf.edu
CONTRACT NUMBER:    AI 43864 (NIAID)
                    AI-41401 (NIAID)
                    AI-43866 (NIAID)
                    P30 MH59037 (NIMH)
SOURCE:             The Journal of infectious diseases, (2002 Feb 1) Vol. 185,
                    No. 3, pp. 315-23.  Electronic Publication: 2002-01-17.
                    Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:        200202
ENTRY DATE:         Entered STN: 28 Jan 2002
                    Last Updated on STN: 5 Jan 2003
                    Entered Medline: 21 Feb 2002
ABSTRACT:
T cell dynamics were studied in human immunodeficiency virus-infected patients
who continued using antiretroviral therapy despite detectable plasma viremia
(RNA copies >2500 /mL).  CD4(+) cell fractional replacement rates, measured by
the deuterated glucose technique, were lower in treated
patients with detectable viremia than in untreated patients and were similar to
those in patients with undetectable viremia.  Cell cycle and activation markers
exhibited similar trends.  For any level of viremia, CD4(+) cell fractional
replacement rates were lower in patients with drug-resistant virus than in
patients with wild-type virus, which suggests that the resistant variant was
less virulent.  Interruption of treatment in patients with drug-resistant
viremia resulted in increased CD4(+) cell activation, increased CD4(+) cell
turnover, and decreased CD4(+) cell counts.  These data indicate that partial
virus suppression reduces CD4(+) cell turnover and activation, thereby
resulting in sustained CD4(+) cell gains, and that measurements of T cell
dynamics may provide an in vivo marker of viral virulence.
CONTROLLED TERM:    Adult
                   *CD4-Positive T-Lymphocytes: IM, immunology
                    CD4-Positive T-Lymphocytes: PH, physiology
                    CD8-Positive T-Lymphocytes: IM, immunology
```

Cell Cycle
Cross-Sectional Studies
Drug Resistance, Viral
HIV Infections: DT, drug therapy
*HIV Infections: IM, immunology
HIV Infections: VI, virology
*HIV Protease Inhibitors: TU, therapeutic use
Humans
Immunophenotyping
*Lymphocyte Activation
RNA, Viral: BL, blood
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*Viremia: IM, immunology

CHEMICAL NAME: 0 (HIV Protease Inhibitors); 0 (RNA, Viral)

L119 ANSWER 2 OF 30 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001549708 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11579235
TITLE: Poor CD4 T cell restoration after suppression of HIV-1 replication may reflect lower thymic function.
AUTHOR: Teixeira L; Valdez H; McCune J M; Koup R A; Badley A D; **Hellerstein M K**; Napolitano L A; Douek D C; Mbisa G; Deeks S; Harris J M; Barbour J D; Gross B H; Francis I R; Halvorsen R; Asaad R; Lederman M M
CORPORATE SOURCE: Division of Infectious Diseases and the Center for AIDS Research, Case Western Reserve University School of Medicine and University Hospitals of Cleveland, Ohio 44106, USA.
CONTRACT NUMBER: AI 36219 (NIAID)
AI35522 (NIAID)
AI41401 (NIAID)
AI43638 (NIAID)
AI43864 (NIAID)
AI43866 (NIAID)
RR-00083 (NCRR)
RR-00088 (NCRR)
SOURCE: AIDS (London, England), (2001 Sep 28) Vol. 15, No. 14, pp. 1749-56.
Journal code: 8710219. ISSN: 0269-9370.
COMMENT: Comment in: AIDS. 2001 Sep 28;15(14):1881-2. PubMed ID: 11579252
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 15 Oct 2001
Last Updated on STN: 22 Feb 2002
Entered Medline: 14 Dec 2001

ABSTRACT:
OBJECTIVE: To characterize immune phenotype and thymic function in HIV-1-infected adults with excellent virologic and poor immunologic responses to highly active antiretroviral therapy (HAART). METHODS: Cross-sectional study of patients with CD4 T cell rises of > or = 200 x 10(6) cells/l (CD4 responders; n = 10) or < 100 x 10(6) cells/l (poor responders; n = 12) in the first year of therapy. RESULTS: Poor responders were older than CD4 responders (46 versus 38 years; P < 0.01) and, before HAART, had higher CD4 cell counts (170 versus 35 x 106 cells/l; P = 0.11) and CD8 cell counts (780 versus 536 x 10(6) cells/l; P = 0.02). After a median of 160 weeks of therapy, CD4

responders had more circulating naive phenotype (CD45+CD62L+) CD4 cells (227 versus 44 x 10(6) cells/l; P = 0.001) and naive phenotype CD8 cells (487 versus 174 x 10(6) cells/l; P = 0.004) than did poor responders (after 130 weeks). Computed tomographic scans showed minimal thymic tissue in 11/12 poor responders and abundant tissue in 7/10 responders (P = 0.006). Poor responders had fewer CD4 cells containing T cell receptor excision circles (TREC) compared with CD4 responders (2.12 versus 27.5 x 10(6) cells/l; P = 0.004) and had shorter telomeres in CD4 cells (3.8 versus 5.3 kb; P = 0.05). Metabolic labeling studies with **deuterated glucose** indicated that the lower frequency of TREC-containing lymphocytes in poor responders was not caused by accelerated proliferation kinetics. CONCLUSION: Poor CD4 T cell increases observed in some patients with good virologic response to HAART may be caused by failure of thymic T cell production.

CONTROLLED TERM: Check Tags: Female; Male
Adult
*Antiretroviral Therapy, Highly Active
CD4-Positive T-Lymphocytes: IM, immunology
*CD4-Positive T-Lymphocytes: PH, physiology
Gene Rearrangement, T-Lymphocyte: GE, genetics
*HIV Infections: DT, drug therapy
HIV Infections: IM, immunology
HIV Infections: VI, virology
*HIV-1: IM, immunology
HIV-1: PH, physiology
Humans
Lymphocyte Subsets
Middle Aged
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Telomere: GE, genetics
*Thymus Gland: PH, physiology
Virus Replication

L119 ANSWER 3 OF 30 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001668112 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11696593
TITLE: Increased turnover of T lymphocytes in HIV-1 infection and its reduction by antiretroviral therapy.
AUTHOR: Mohri H; Perelson A S; Tung K; Ribeiro R M; Ramratnam B; Markowitz M; Kost R; Hurley A; Weinberger L; Cesar D; **Hellerstein M K**; Ho D D
CORPORATE SOURCE: Aaron Diamond AIDS Research Center, The Rockefeller University, New York, NY 10016, USA.
CONTRACT NUMBER: AI40387 (NIAID)
AI42848 (NIAID)
SOURCE: The Journal of experimental medicine, (2001 Nov 5) Vol. 194, No. 9, pp. 1277-87.
Journal code: 2985109R. ISSN: 0022-1007.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 21 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 18 Dec 2001

ABSTRACT:
The mechanism of CD4(+) T cell depletion in human immunodeficiency virus (HIV)-1 infection remains controversial. Using **deuterated** ***glucose*** to label the DNA of proliferating cells in vivo, we studied T

cell dynamics in four normal subjects and seven HIV-1-infected patients naive to antiretroviral drugs. The results were analyzed using a newly developed mathematical model to determine fractional rates of lymphocyte proliferation and death. In CD4(+) T cells, mean proliferation and death rates were elevated by 6.3- and 2.9-fold, respectively, in infected patients compared with normal controls. In CD8(+) T cells, the mean proliferation rate was 7.7-fold higher in HIV-1 infection, but the mean death rate was not significantly increased. Five of the infected patients underwent subsequent **deuterated** ***glucose*** labeling studies after initiating antiretroviral therapy. The lymphocyte proliferation and death rates in both CD4(+) and CD8(+) cell populations were substantially reduced by 5-11 weeks and nearly normal by one year. Taken together, these new findings strongly indicate that CD4(+) lymphocyte depletion seen in AIDS is primarily a consequence of increased cellular destruction, not decreased cellular production.

CONTROLLED TERM: Check Tags: Female; Male
Adult
Apoptosis: IM, immunology
CD4 Lymphocyte Count
CD4-Positive T-Lymphocytes: CY, cytology
*CD4-Positive T-Lymphocytes: IM, immunology
CD8-Positive T-Lymphocytes: CY, cytology
*CD8-Positive T-Lymphocytes: IM, immunology
Cell Division
Gene Expression
HIV Infections: DT, drug therapy
*HIV Infections: IM, immunology
HIV Infections: VI, virology
*HIV-1: IM, immunology
Health Status
Humans
In Situ Nick-End Labeling
Ki-67 Antigen: GE, genetics
Ki-67 Antigen: IM, immunology
Kinetics
Longitudinal Studies
Middle Aged
Monocytes: CY, cytology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Time Factors
Viral Load

CHEMICAL NAME: 0 (Ki-67 Antigen)

L119 ANSWER 4 OF 30 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 2000177756 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10712441

TITLE: Factors influencing T-cell turnover in HIV-1-seropositive patients.

AUTHOR: McCune J M; Hanley M B; Cesar D; Halvorsen R; Hoh R; Schmidt D; Wieder E; Deeks S; Siler S; Neese R; **Hellerstein M**

CORPORATE SOURCE: The Gladstone Institute of Virology and Immunology, University of California-San Francisco, San Francisco, California 94141, USA.. mmccune@gladstone.ucsf.edu

CONTRACT NUMBER: AI40312 (NIAID)
AI43864 (NIAID)
AI43866 (NIAID)
+

SOURCE: The Journal of clinical investigation, (2000 Mar) Vol. 105, No. 5, pp. R1-8.

Journal code: 7802877. ISSN: 0021-9738.
COMMENT: Comment in: J Clin Invest. 2000 Mar;105(5):565-6. PubMed ID: 10712427
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 7 Apr 2000
Last Updated on STN: 27 Dec 2002
Entered Medline: 30 Mar 2000

ABSTRACT:
HIV-1 disease is associated with pathological effects on T-cell production, destruction, and distribution. Using the **deuterated** (2H) ***glucose*** method for endogenous labeling, we have analyzed host factors that influence T-cell turnover in HIV-1-uninfected and -infected humans. In untreated HIV-1 disease, the average half life of circulating T cells was diminished without compensatory increases in cell production. Within 12 weeks of the initiation of highly active antiretroviral therapy (HAART), the absolute production rates of circulating T cells increased, and normal half-lives and production rates were restored by 12-36 months. Interpatient heterogeneity in the absolute degree of turnover correlated with the relative proportion of naive- and memory/effector-phenotype T cells in each of the CD4+ and CD8+ populations. The half-lives of naive-phenotype T cells ranged from 116-365 days (fractional replacement rates of 0.19-0.60% per day), whereas memory/effector-phenotype T cells persisted with half-lives from 22-79 days (fractional replacement rates of 0.87-3.14% per day). Naive-phenotype T cells were more abundant, and the half-life of total T cells was prolonged in individuals with abundant thymic tissue, as assessed by computed tomography. Such interpatient variation in T-cell kinetics may be reflective of differences in functional immune reconstitution after treatment for HIV-1 disease.

CONTROLLED TERM:
CD4-Positive T-Lymphocytes: ME, metabolism
CD4-Positive T-Lymphocytes: VI, virology
CD8-Positive T-Lymphocytes: ME, metabolism
CD8-Positive T-Lymphocytes: VI, virology
Cell Count
Cell Survival
Deuterium
Flow Cytometry
Glucose: ME, metabolism
HIV Infections: DT, drug therapy
*HIV Infections: IM, immunology
*HIV-1: IM, immunology
Humans
Kinetics
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*T-Lymphocytes: ME, metabolism
T-Lymphocytes: VI, virology
Thymus Gland: PA, pathology
Tomography, X-Ray Computed

CAS REGISTRY NO.: 50-99-7 (Glucose); 7782-39-0 (Deuterium)

L119 ANSWER 5 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2001013497 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10895854
TITLE: Effect of pinitol treatment on insulin action in subjects with insulin resistance.
AUTHOR: Davis A; Christiansen M; Horowitz J F; Klein S; **Hellerstein M K**; Ostlund R E Jr

CORPORATE SOURCE: Department of Pediatrics, Washington University School of Medicine, St Louis, Missouri 63110, USA..
davis_a@kids.wustl.edu
CONTRACT NUMBER: AG 00078 (NIA)
RR 00036 (NCRR)
RR 00954 (NCRR)
SOURCE: Diabetes care, (2000 Jul) Vol. 23, No. 7, pp. 1000-5.
Journal code: 7805975. ISSN: 0149-5992.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 30 Oct 2000

ABSTRACT:
OBJECTIVE: Endogenous low-molecular-weight glycans containing pinitol (3-O-methyl-D-chiro-inositol) and D-chiro-inositol are thought to mediate certain actions of insulin. We tested the hypothesis that oral administration of soybean-derived pinitol would improve insulin sensitivity in obese subjects (BMI = 36.6 kg/m2) with diet-treated type 2 diabetes or glucose intolerance (HbA1c = 6.8%). RESEARCH DESIGN AND METHODS: There were 22 subjects randomized to receive either pinitol 20 mg x kg(-1) x day(-1) (n = 12) or placebo (n = 10) in a 28-day double-blinded trial. RESULTS: No toxicity due to the pinitol was observed during the study The sensitivity of glucose and lipid metabolism to insulin were assessed by measurement of whole-body glucose, palmitate, and glycerol kinetics during basal conditions and a hyperinsulinemic-euglycemic clamp. Metabolic measurements were made at baseline and again at the end of the study Final plasma levels of pinitol were 48-fold (1.06 +/- 0.15 vs. 0.02 +/- 0.01 micromol/l, P < 0.0001) and D-chiro-inositol levels 14-fold (0.56 +/- 0.08 vs. 0.04 +/- 0.02 micromol/l, P < 0.0001) greater in the pinitol group compared with placebo. CONCLUSIONS: Four weeks of pinitol treatment did not alter baseline glucose production, insulin-mediated glucose disposal, or rates of appearance of free fatty acids and glycerol in plasma. We conclude that plasma levels of both pinitol and D-chiro-inositol are very responsive to pinitol ingestion, but insulin sensitivity does not increase after pinitol treatment in individuals with obesity and mild type 2 diabetes.

CONTROLLED TERM: Check Tags: Female; Male
Blood Glucose: DE, drug effects
*Blood Glucose: ME, metabolism
*Diabetes Mellitus: DT, drug therapy
Diabetes Mellitus, Type 2: BL, blood
*Diabetes Mellitus, Type 2: DT, drug therapy
Diabetes Mellitus, Type 2: PP, physiopathology
Double-Blind Method
Glucose Clamp Technique
Glucose Intolerance: BL, blood
*Glucose Intolerance: DT, drug therapy
Glucose Intolerance: PP, physiopathology
Humans
Hyperinsulinism
Infusions, Intravenous
Inositol: AE, adverse effects
*Inositol: AA, analogs & derivatives
Inositol: PK, pharmacokinetics
*Inositol: TU, therapeutic use

Insulin: AD, administration & dosage
Insulin: PD, pharmacology
***Insulin Resistance**
Middle Aged
Obesity: BL, blood
*Obesity: DT, drug therapy
Obesity: PP, physiopathology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
CAS REGISTRY NO.: 11061-68-0 (Insulin); 484-68-4 (pinitol); 6917-35-7 (Inositol)
CHEMICAL NAME: 0 (Blood Glucose)

L119 ANSWER 6 OF 30 MEDLINE on STN
ACCESSION NUMBER: 2000123707 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10648253
TITLE: Carbohydrate-induced hypertriacylglycerolemia: historical perspective and review of biological mechanisms.
AUTHOR: Parks E J; **Hellerstein M K**
CORPORATE SOURCE: Department of Food Science and Nutrition, University of Minnesota-Twin Cities, St Paul, MN 55108-6099, USA.. eparks@tc.umn.edu
SOURCE: The American journal of clinical nutrition, (2000 Feb) Vol. 71, No. 2, pp. 412-33. Ref: 190
Journal code: 0376027. ISSN: 0002-9165.
COMMENT: Comment in: Am J Clin Nutr. 2001 Jan;73(1):129-30. PubMed ID: 11124766
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 29 Feb 2000
Last Updated on STN: 8 May 2002
Entered Medline: 17 Feb 2000

ABSTRACT:
Current trends in health promotion emphasize the importance of reducing dietary fat intake. However, as dietary fat is reduced, the dietary carbohydrate content typically rises and the desired reduction in plasma cholesterol concentrations is frequently accompanied by an elevation of plasma triacylglycerol. We review the phenomenon of carbohydrate-induced hypertriacylglycerolemia, the health effects of which are among the most controversial and important issues in public health nutrition today. We first focus on how seminal observations made in the late 1950s and early 1960s became the basis for subsequent important research questions and areas of scientific study. The second focus of this paper is on the current knowledge of biological mechanisms that contribute to carbohydrate-induced hypertriacylglycerolemia. The clinical rationale behind mechanistic studies is this: if carbohydrate-induced hypertriacylglycerolemia shares a metabolic basis with endogenous hypertriacylglycerolemia (that observed in subjects consuming high-fat diets), then a similar atherogenic risk may be more likely than if the underlying metabolic mechanisms differ. The third focus of the paper is on both the positive metabolic changes that occur when high-carbohydrate diets are consumed and the potentially negative health effects of such diets. The review concludes with a summary of some important research questions that remain to be addressed. These issues include the level of dietary carbohydrate that induces carbohydrate-induced hypertriacylglycerolemia, whether the phenomenon is transient or can be avoided, whether de novo lipogenesis contributes to the phenomenon, and what magnitude of triacylglycerol elevation represents an

increase in disease risk.

CONTROLLED TERM: Apolipoproteins B: BL, blood
Chylomicrons: BL, blood
Dietary Carbohydrates: AD, administration & dosage
*Dietary Carbohydrates: PD, pharmacology
Dietary Fats: AD, administration & dosage
Humans
Hyperlipoproteinemia: BL, blood
Insulin Resistance
Lipoprotein Lipase: ME, metabolism
Lipoproteins, VLDL: BL, blood
Obesity: BL, blood
Research Support, Non-U.S. Gov't
Risk Factors
*Triglycerides: BL, blood

CHEMICAL NAME: 0 (Apolipoproteins B); 0 (Chylomicrons); 0 (Dietary Carbohydrates); 0 (Dietary Fats); 0 (Lipoproteins, VLDL); 0 (Triglycerides); 0 (very low density lipoprotein triglyceride); EC 3.1.1.34 (Lipoprotein Lipase)

L119 ANSWER 7 OF 30 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:14457 BIOSIS Full-text

DOCUMENT NUMBER: PREV200600017490

TITLE: The **deuterated-glucose** disposal test (GDT): A sensitive, high-throughput measure of insulin resistance in vivo.

AUTHOR(S): Beysen, Carine [Reprint Author]; Murphy, Elizabeth J.; Awada, Mohamad; Turner, Holly; Riff, Tim J.; Turner, Scott M.; **Hellerstein, Marc K.**

SOURCE: Diabetes, (2005) Vol. 54, No. Suppl. 1, pp. A152.
Meeting Info.: 65th Annual Meeting of the American-Diabetes-Association. San Diego, CA, USA. June 10 -14, 2005. Amer Diabet Assoc.
CODEN: DIAEAZ. ISSN: 0012-1797.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Dec 2005
Last Updated on STN: 21 Dec 2005

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Pathology - Therapy 12512
Metabolism - General metabolism and metabolic pathways 13002
Metabolism - Metabolic disorders 13020
Nutrition - Malnutrition and obesity 13203
Digestive system - Physiology and biochemistry 14004
Endocrine - General 17002
Endocrine - Pancreas 17008
Pharmacology - Drug metabolism and metabolic stimulators 22003

INDEX TERMS: Major Concepts
Methods and Techniques; Metabolism; Endocrine System (Chemical Coordination and Homeostasis)

INDEX TERMS: Parts, Structures, & Systems of Organisms
pancreas: endocrine system, digestive system

INDEX TERMS: Diseases

obesity: nutritional disease
Obesity (MeSH)

INDEX TERMS: Diseases
insulin resistance: endocrine disease/pancreas, metabolic disease
Insulin Resistance (MeSH)

INDEX TERMS: Chemicals & Biochemicals
insulin; glucose: oxidation; rosiglitazone: metabolic-drug

INDEX TERMS: Methods & Equipment
deuterated-glucose disposal test [GDT]: clinical techniques, diagnostic techniques

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Sprague-Dawley rat (common)
Zucker rat (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 9004-10-8 (insulin)
58367-01-4 (glucose)
122320-73-4 (rosiglitazone)

L119 ANSWER 8 OF 30 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:154245 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600162069
TITLE: A new, sensitive in vivo diagnostic test of insulin resistance: The **deuterated** oral **glucose** tolerance test (H-2-OGTT).
AUTHOR(S): Murphy, Elizabeth J. [Reprint Author]; Turner, Scott M.; LaPrade, Kristen; Neese, Richard A.; Bohan, DrinA I.; **Hellerstein, Marc K.**
SOURCE: Diabetes, (JUN 2004) Vol. 53, No. Suppl. 2, pp. A158-A159. Meeting Info.: 64th Annual Meeting of the American-Diabetes-Association. Orlando, FL, USA. June 04 -08, 2004. Amer Diabet Assoc.
CODEN: DIAEAZ. ISSN: 0012-1797.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Mar 2006
Last Updated on STN: 9 Mar 2006
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Pathology - Therapy 12512
Metabolism - Metabolic disorders 13020
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Endocrine - General 17002
Endocrine - Pancreas 17008
Pharmacology - General 22002
Pharmacology - Clinical pharmacology 22005
Pharmacology - Immunological processes and allergy 22018

Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508

INDEX TERMS: Major Concepts
Pharmacology; Clinical Immunology (Human Medicine, Medical Sciences); Clinical Endocrinology (Human Medicine, Medical Sciences)

INDEX TERMS: Parts, Structures, & Systems of Organisms
T cell: immune system, blood and lymphatics

INDEX TERMS: Diseases
type 1 diabetes: endocrine disease/pancreas, immune system disease, metabolic disease, immunology
Diabetes Mellitus, Insulin-Dependent (MeSH)

INDEX TERMS: Chemicals & Biochemicals
interferon-gamma; FasL; IL-10 [interleukin-10]; TNF-alpha [tumor necrosis factor-alpha]; IL-6 [interleukin-6]; CD80; T-bet; CD154; anti-CD3 antibody; anti-CD28 antibody; GrB; interferon alpha: immunologic-drug, oral administration, dose

INDEX TERMS: Methods & Equipment
quantitative real time PCR: laboratory techniques, genetic techniques

INDEX TERMS: Miscellaneous Descriptors
disease onset

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L119 ANSWER 9 OF 30 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:458381 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300458381
TITLE: Subpopulations of long-lived and short-lived T cells in advanced HIV-1 infection.
AUTHOR(S): **Hellerstein, Marc K.** [Reprint Author]; Hoh, Rebecca A.; Hanley, Mary Beth; Cesar, Denise; Lee, Daniel; Neese, Richard A.; McCune, Joseph M.
CORPORATE SOURCE: University of California, Berkeley, 119 Morgan Hall, Berkeley, CA, 94720-3104, USA
march@nature.berkeley.edu
SOURCE: Journal of Clinical Investigation, (September 2003) Vol. 112, No. 6, pp. 956-966. print.
CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 2003
Last Updated on STN: 8 Oct 2003

ABSTRACT:Antigenic stimulation of T cells gives rise to short-lived effector cells and long-lived memory cells. We used two stable isotope-labeling techniques to identify kinetically distinct subpopulations of T cells and to determine the effect of advanced infection with HIV-1. Long-term deuterated water (2H2O) incorporation into DNA demonstrated biphasic accrual of total and of memory/effector (m/e)-phenotype but not naive-phenotype T cells, consistent with the presence of short-lived and longer-lived subpopulations within the m/e-phenotype T cell pool. These results were mirrored by biphasic die-away kinetics in m/e- but not naive-phenotype T cells after short-term 2H-glucose

labeling. Persistent label retention was observed in a subset of m/e-phenotype T cells (presumably memory T cells), confirming the presence of T cells with very different life spans in humans. In advanced HIV-1 infection, much higher proportions of T cells were short-lived, compared to healthy controls. Effective long-term anti-retroviral therapy restored values to normal. These results provide the first quantitative evidence that long-lived and quiescent T cells do indeed predominate in the T cell pool in humans and determine T cell pool size, as in rodents. The greatest impact of advanced HIV-1 infection is to reduce the generation of long-lived, potential progenitor T cells.

CONCEPT CODE:
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Virology - General and methods 33502
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - General and methods 36001
Medical and clinical microbiology - Virology 36006

INDEX TERMS:
Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection

INDEX TERMS:
Parts, Structures, & Systems of Organisms
CD4 positive T cell: immune system; CD8 positive T cell: immune system; T cell: blood and lymphatics, immune system, long-lived, short-lived, subpopulations

INDEX TERMS:
Diseases
HIV-1 infection: immune system disease, infectious disease, viral disease, human immunodeficiency virus 1 infection
HIV Infections (MeSH)

INDEX TERMS:
Chemicals & Biochemicals
DNA; **[deuterated]-glucose**; deuterated water

INDEX TERMS:
Methods & Equipment
anti-retroviral therapy: clinical techniques, therapeutic and prophylactic techniques; gas chromatography-mass spectrometry [GC/MS]: chromatographic techniques, laboratory techniques, spectrum analysis techniques; isotope-labeling technique: laboratory techniques

ORGANISM:
Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): host
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM:
Classifier
Retroviridae 03305
Super Taxa
DNA and RNA Reverse Transcribing Viruses; Viruses; Microorganisms
Organism Name
HIV-1 (miscellaneous) [Human immunodeficiency virus 1 (species)]: pathogen

Taxa Notes
DNA and RNA Reverse Transcribing Viruses, Microorganisms, Viruses
REGISTRY NUMBER: 7789-20-0 (deuterated water)

L119 ANSWER 10 OF 30 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:318745 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100318745
TITLE: Measurements of in vivo proliferation kinetics of human marrow CD34+ cells by quantitating 2(H)-glucose incorporation into DNA of S-phase cells.
AUTHOR(S): Schwartz, Gretchen N. [Reprint author]; Vance, Barbara A. [Reprint author]; Fukazawa, Motoharu [Reprint author]; Telford, William G. [Reprint author]; Levine, Benjamin M. [Reprint author]; Cesar, Denise; **Hellerstein, Marc K.**; Gress, Ronald E. [Reprint author]
CORPORATE SOURCE: Medicine Branch, National Cancer Institute, Bethesda, MD, USA
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 662a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002

ABSTRACT:Previous results demonstrated that after recovery from chemotherapy normal blood cell counts are maintained even though marrow hematopoietic progenitor numbers or functions are suppressed. One possible mechanism for the maintenance of normal blood cell levels is a change in the proliferation kinetics of committed or primitive progenitors or their precursors. In this report, the feasibility of using a recently developed in vivo ***deuterated*** **glucose** (2(H)-glucose) labeling approach (Hellerstein et al., PNAS 95:708, 1998) to measure proliferation kinetics of CD34+ cells in marrow from normal donors was investigated. With this approach, infused 2(H)-glucose becomes incorporated into DNA of all S-phase cells through the de novo nucleotide synthesis pathway. Normal donors were administered a 48 hour infusion of 2(H)-glucose and marrow aspirates were obtained 0 to 24 hours, two weeks, and four weeks following cessation of the infusion. Marrow samples were enriched for CD34+ cells (> 95%), DNA was isolated, derivatized, and analyzed by gas chromatography/mass spectrometry for enrichment of 2(H)-dexoxyadenosine (%dA). The %dA enrichment was used to calculate the percentage of newly synthesized cells, the rate of new cell production (i.e., k/day) during the infusion period, and the rate labeled cells were lost (k-decay). After a 48 hour infusion, 44 +- 1.4% (mean +- s.e.m., n = 7 donors) of CD34+ cells were newly synthesized with a replacement rate constant, k = 0.29 +- 0.1/day and a t1/2 of 2.4 +- 0.11 days. In the interval from zero to two weeks there was a significant loss of label in total CD34+ cells with a t1/2 decay = 3.8 days. There was an additional slower loss of label from two to four weeks with a t1/2 decay = 10.2 days. In preliminary results, after a 48 hour infusion of 2(H)-glucose, 29% of AC133+ cells (a subset of CD34+ cells enriched for primitive progenitors) and 50% of AC133- cells in the marrow were new cells. The results suggest the presence of subpopulations of CD34+ cells with different proliferation kinetics. The results demonstrate that in vivo labeling with 2(H)-glucose provides a sensitive and reproducible method to measure proliferation kinetics of subpopulations of CD34+ cells and provide

baseline data for patient chemotherapy and transplantation studies. These results are the first known determinations of in vivo CD34+ cell half-life in humans.

CONCEPT CODE: Blood - Blood and lymph studies 15002
General biology - Symposia, transactions and proceedings 00520
Cytology - Animal 02506
Cytology - Human 02508
Biochemistry studies - Nucleic acids, purines and pyrimidines 10062
Blood - Blood cell studies 15004
Immunology - General and methods 34502

INDEX TERMS: Major Concepts
Methods and Techniques; Blood and Lymphatics (Transport and Circulation)

INDEX TERMS: Parts, Structures, & Systems of Organisms
CD34-positive cells: blood and lymphatics, immune system, proliferation; bone marrow: blood and lymphatics, immune system

INDEX TERMS: Chemicals & Biochemicals
DNA; **[deuterated]glucose**: incorporation

INDEX TERMS: Methods & Equipment
[deuterated]glucose labeling: analytical method

INDEX TERMS: Miscellaneous Descriptors
cell cycle; Meeting Abstract

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

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ACCESSION NUMBER: 2000352156 EMBASE Full-text
TITLE: Effect of dietary energy restriction on **glucose** production and substrate utilization in type 2 diabetes.
AUTHOR: Christiansen M.P.; Linfoot P.A.; Neese R.A.; **Hellerstein M.K.**
CORPORATE SOURCE: Dr. M.K. Hellerstein, Department of Nutritional Sciences, 309 Morgan Hall, University of California, Berkeley, CA 94720-3104, United States. march@nature.berkeley.edu
SOURCE: Diabetes, (2000) Vol. 49, No. 10, pp. 1691-1699. .
Refs: 42
ISSN: 0012-1797 CODEN: DIAEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 26 Oct 2000
Last Updated on STN: 26 Oct 2000

ABSTRACT: A total of 8 obese subjects with type 2 diabetes were studied while on a eucaloric diet and after reduced energy intake (25 and then 75% of

requirements for 10 days each). Weight loss was 2, 3, and 3 kg after 5, 10, and 20 days, respectively; all of the weight lost was body fat. Fasting blood ***glucose*** (FBG) levels fell from 11.9 ± 1.4 at baseline to 8.9 ± 1.6, 7.9 ± 1.4, and 8.8 ± 1.3 mmol/l at days 5, 10, and 20, respectively ($P < 0.05$, baseline vs. 5, 10, and 20 days). Endogenous **glucose** production (EGP) was 22 ± 2, 18 ± 2, 17 ± 2, and 22 ± 2 μmol · kg-1 lean body mass (LBM) · min-1 ($P < 0.05$, days 5 and 10 vs. baseline). Gluconeogenesis measured by mass isotopomer distribution analysis provided 31 ± 4, 41 ± 5, 40 ± 4, and 33 ± 4%, respectively, of the EGP (NS); absolute glycogenolytic contribution to the EGP was 15 ± 2, 11 ± 2, 11 ± 2, and 15 ± 2 μmol · kg-1 LBM min-1, respectively ($P < 0.001$, baseline vs. days 5 and 10 and day 10 vs. day 20). The blood ***glucose*** clearance rate increased significantly at day 20 ($P < 0.05$). Neither lipolysis nor flux of plasma nonesterified fatty acids were altered compared with baseline. In conclusion, severe energy restriction per se independent of major changes in body composition reduces both FBG concentration and EGP in type 2 diabetes, the reduction in EGP results entirely from a reduction of glycogenolytic input into blood **glucose**, and the duration of reduced glycogenolysis is short-lived after relaxation of energy restriction even without weight gain, but effects on plasma **glucose** clearance persist and partially maintain the improvement in fasting glycemia.

CONTROLLED TERM: Medical Descriptors:
***obesity**
*non insulin dependent diabetes mellitus
*caloric restriction
*gluconeogenesis
weight reduction
body fat
glucose blood level
lean body weight
glycogenolysis
metabolic clearance rate
lipolysis
fatty acid blood level
weight gain
human
male
female
clinical article
adult
article
priority journal
Drug Descriptors:
***glucose: EC, endogenous compound**
*fatty acid: EC, endogenous compound

CAS REGISTRY NO.: (**glucose**) **50-99-7**, 84778-64-3

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ACCESSION NUMBER: 2000147267 EMBASE Full-text
TITLE: Relationship between carbohydrate-induced hypertriglyceridemia and fatty acid synthesis in lean and obese subjects.
AUTHOR: Hudgins L.G.; **Hellerstein M.K.**; Seidman C.E.; Neese R.A.; Tremaroli J.D.; Hirsch J.
CORPORATE SOURCE: L.G. Hudgins, Rogosin Institute, Box 72, Rockefeller University, New York, NY, United States
SOURCE: Journal of Lipid Research, (2000) Vol. 41, No. 4, pp. 595-604. .

Refs: 45
ISSN: 0022-2275 CODEN: JLPRAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 May 2000
Last Updated on STN: 11 May 2000

ABSTRACT: We previously reported that a eucaloric, low fat, liquid formula diet enriched in simple carbohydrate markedly increased the synthesis of fatty acids in lean volunteers. To examine the diet sensitivity of obese subjects, 7 obese and 12 lean volunteers were given two eucaloric low fat solid food diets enriched in simple sugars for 2 weeks each in a random-order, cross- over design (10% fat, 75% carbohydrate vs. 30% fat, 55% carbohydrate, ratio of sugar to starch 60:40). The fatty acid compositions of both diets were matched to the composition of each subject's adipose tissue and fatty acid synthesis measured by the method of linoleate dilution in plasma VLDL triglyceride. In all subjects, the maximum % de novo synthesized fatty acids in VLDL trigiyceride 3-9 h after the last meal was higher on the 10% versus the 30% fat diet. There was no significant difference between the dietary effects on lean (43 ± 13 vs. 12 ± 13%) and obese (37 ± 15 vs. 6 ± 6%) subjects, despite 2-fold elevated levels of insulin and reduced glucagon levels in the obese. Similar results were obtained for de novo palmitate synthesis in VLDL triglyceride measured by mass isotopomer distribution analysis after infusion of [13C]acetate. On the 10% fat diet, plasma triglycerides (fasting and 24 h) were increased and correlated with fatty acid synthesis. Triglycerides were higher when fatty acid synthesis was constantly elevated rather than having diurnal variation. Thus, eucaloric, solid food diets which are very low in fat and high in simple sugars markedly stimulate fatty acid synthesis from carbohydrate, and plasma triglycerides increase in proportion to the amount of fatty acid synthesis. However, this dietary effect is not related to body mass index, insulin, or glucagon levels.

CONTROLLED TERM: Medical Descriptors:
***obesity: ET, etiology**
*hypertriglyceridemia
*carbohydrate intake
*fatty acid synthesis
hyperlipidemia
lipogenesis
triacylglycerol blood level
lipid blood level
body mass
calorimetry
energy expenditure
human
male
female
clinical article
adult
article
priority journal
Drug Descriptors:
*triacylglycerol
*palmitic acid
*linoleic acid

*very low density lipoprotein cholesterol
fatty acid
acetic acid
carbon 13
high density lipoprotein cholesterol
glucose
glucagon
insulin

CAS REGISTRY NO.: (palmitic acid) 57-10-3; (linoleic acid) 1509-85-9, 2197-37-7, 60-33-3, 822-17-3; (acetic acid) 127-08-2, 127-09-3, 64-19-7, 71-50-1; (carbon 13) 14762-74-4; (**glucose**) **50-99-7**, 84778-64-3; (glucagon) 11140-85-5, 62340-29-8, 9007-92-5; (insulin) 9004-10-8

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ACCESSION NUMBER: 2003371079 EMBASE Full-text

TITLE: Turnover of adipose components and mitochondrial DNA in humans: Kinetic biomarkers for human immunodeficiency virus - Associated lipodystrophy and mitochondrial toxicity?.

AUTHOR: **Hellerstein M.K.**

CORPORATE SOURCE: Dr. M.K. Hellerstein, Dept. of Nutritional Sci./Toxicology, 309 Morgan Hall, University of California, Berkeley, CA 94720-3104, United States. march@nature.berkeley.edu

SOURCE: Clinical Infectious Diseases, (1 Sep 2003) Vol. 37, No. SUPPL. 2, pp. S52-S61. .
Refs: 40
ISSN: 1058-4838 CODEN: CIDIEL

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 003 Endocrinology
004 Microbiology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 2 Oct 2003
Last Updated on STN: 2 Oct 2003

ABSTRACT: Lipoatrophy (LA)/lipodystrophy and nucleoside reverse-transcriptase inhibitor (NRTI)-associated syndrome are of central importance in human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) care. Neither of these conditions has had a clear pathogenesis or biomarker defined for early detection, prevention research, or patient management. I describe the recent development of kinetic biomarkers for LA and mitochondrial toxicity that involve the measurement of biosynthetic fluxes rather than static concentrations of molecules. The turnover of adipose-tissue components (lipids and cells) and tissue mitochondrial DNA is measured by the incorporation of deuterium from heavy water, using mass spectrometry. Preliminary results in animal models and humans, including the effects of NRTIs on mitochondrial DNA synthesis in rats and adipose-tissue lipid kinetics in HIV-associated LA, are reviewed. The results suggest that the kinetics of adipose-tissue components and mitochondrial DNA are measurable in vivo and that these measurements may prove useful as clinical biomarkers in patients with HIV/AIDS.

CONTROLLED TERM: Medical Descriptors:
*Human immunodeficiency virus infection: ET, etiology
*lipodystrophy
*mitochondrion
*adipose tissue
pathogenesis
lipoatrophy

disease association
Human immunodeficiency virus
acquired immune deficiency syndrome: ET, etiology
virus detection
mass spectrometry
DNA synthesis
kinetics
turnover time
body fat
lipolysis
adipocyte
cell division
DNA replication
cell proliferation
mutagenicity
T lymphocyte
B lymphocyte
skin epithelium
liver cell
monocyte
breast cancer
granulocyte
natural killer cell
hematopoietic stem cell
muscle cell
lipid metabolism
lipogenesis
obesity
food intake
energy expenditure
insulin resistance
fat necrosis
gene expression
reverse transcription polymerase chain reaction
biogenesis
thrombocyte
DNA isolation
glucose blood level
drug screening
liver
hyperphagia
human
nonhuman
review
priority journal
Drug Descriptors:
*mitochondrial DNA: EC, endogenous compound
biological marker: EC, endogenous compound
deuterium
deuterium oxide
RNA directed DNA polymerase inhibitor: PD, pharmacology
triacylglycerol: EC, endogenous compound
tracer
fatty acid: EC, endogenous compound
glucose: EC, endogenous compound
thymidine
broxuridine
leptin: PD, pharmacology
leptin: SC, subcutaneous drug administration
insulin: EC, endogenous compound

peroxisome proliferator activated receptor gamma: EC, endogenous compound
zidovudine: PD, pharmacology
zidovudine: PO, oral drug administration
muscle protein: EC, endogenous compound
glycosylated hemoglobin: EC, endogenous compound
hemoglobin C: EC, endogenous compound
messenger RNA: EC, endogenous compound
DNA polymerase: EC, endogenous compound

CAS REGISTRY NO.: (deuterium) 7782-39-0; (deuterium oxide) 11105-15-0, 13587-54-7, 7789-20-0; (**glucose**) **50-99-7**, 84778-64-3; (thymidine) 50-89-5; (broxuridine) 59-14-3; (insulin) 9004-10-8; (zidovudine) 30516-87-1; (glycosylated hemoglobin) 9062-63-9; (hemoglobin C) 9008-00-8; (DNA polymerase) 37217-33-7

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ACCESSION NUMBER: 2000098765 EMBASE Full-text

TITLE: Factors influencing T-cell turnover in HIV-1-seropositive patients.

AUTHOR: McCune J.M.; Hanley M.B.; Cesar D.; Halvorsen R.; Hoh R.; Schmidt D.; Wieder E.; Deeks S.; Siler S.; Neese R.; **Hellerstein M.**

CORPORATE SOURCE: J.M. McCune, Gladstone Inst. of Virology/Immunol., Univ. of California-San Francisco, PO Box 419100, San Francisco, CA 94141-9100, United States. mmccune@gladstone.ucsf.edu

SOURCE: Journal of Clinical Investigation, (2000) Vol. 105, No. 5, pp. R1-R8. .
Refs: 29
ISSN: 0021-9738 CODEN: JCINAO

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 30 Mar 2000
Last Updated on STN: 30 Mar 2000

ABSTRACT: HIV-1 disease is associated with pathological effects on T-cell production, destruction, and distribution. Using the **deuterated** (2H) ***glucose*** method for endogenous labeling, we have analyzed host factors that influence T-cell turnover in HIV-1-uninfected and -infected humans. In untreated HIV-1 disease, the average half life of circulating T cells was diminished without compensatory increases in cell production. Within 12 weeks of the initiation of highly active antiretroviral therapy (HAART), the absolute production rates of circulating T cells increased, and normal half-lives and production rates were restored by 12-36 months. Interpatient heterogeneity in the absolute degree of turnover correlated with the relative proportion of naive- and memory/effector-phenotype T cells in each of the CD4+ and CD8+ populations. The half-lives of naive-phenotype T cells ranged from 116-365 days (fractional replacement rates of 0.19-0.60% per day), whereas memory/effector-phenotype T cells persisted with half-lives from 22-79 days (fractional replacement rates of 0.87-3.14% per day). Naive-phenotype T cells were more abundant, and the half-life of total T cells was prolonged in individuals with abundant thymic tissue, as assessed by computed tomography. Such interpatient variation in T-cell kinetics may be reflective of differences in functional immune reconstitution after treatment for HIV-1 disease.

CONTROLLED TERM: Medical Descriptors:

*Human immunodeficiency virus 1
*lymphocytopoiesis
Human immunodeficiency virus infection
T lymphocyte
half life time
lymphocyte count
virus replication
human
male
female
clinical article
controlled study
human cell
article
priority journal

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ACCESSION NUMBER: 1999163890 EMBASE Full-text
TITLE: De novo lipogenesis in humans: Metabolic and regulatory aspects.
AUTHOR: **Hellerstein M.K.**
CORPORATE SOURCE: M.K. Hellerstein, Department of Nutritional Sciences, University of California at Berkeley, Berkeley, CA 94270-3104, United States
SOURCE: European Journal of Clinical Nutrition, (1999) Vol. 53, No. SUPPL. 1, pp. S53-S65. .
Refs: 83
ISSN: 0954-3007 CODEN: EJCNEQ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 27 May 1999
Last Updated on STN: 27 May 1999

ABSTRACT: The enzymatic pathway for converting dietary carbohydrate (CHO) into fat, or de novo lipogenesis (DNL), is present in humans, whereas the capacity to convert fats into CHO does not exist. Here, the quantitative importance of DNL in humans is reviewed, focusing on the response to increased intake of dietary CHO. Eucaloric replacement of dietary fat by CHO does not induce hepatic DNL to any substantial degree. Similarly, addition of CHO to a mixed diet does not increase hepatic DNL to quantitatively important levels, as long as CHO energy intake remains less than total energy expenditure (TEE). Instead, dietary CHO replaces fat in the whole-body fuel mixture, even in the post-absorptive state. Body fat is thereby accrued, but the pathway of DNL is not traversed; instead, a coordinated set of metabolic adaptations, including resistance of hepatic **glucose** production to suppression by insulin, occurs that allows CHO oxidation to increase and match CHO intake. Only when CHO energy intake exceeds TEE does DNL in liver or adipose tissue contribute significantly to the wholebody energy economy. It is concluded that DNL is not the pathway of first resort for added dietary CHO, in humans. Under most dietary conditions, the two major macronutrient energy sources (CHO and fat) are therefore not interconvertible currencies; CHO and fat have independent, though interacting, economies and independent regulation. The metabolic mechanisms and physiologic implications of the functional block between CHO and fat in humans are discussed, but require further investigation.

CONTROLLED TERM: Medical Descriptors:

*lipogenesis
*carbohydrate diet
fat intake
caloric intake
energy expenditure
body fat
gluconeogenesis
enzyme activity
obesity
diabetes mellitus
human
male
female
conference paper

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ACCESSION NUMBER: 1998038284 EMBASE Full-text
TITLE: Contribution of newly synthesized cholesterol to rat plasma and bile determined by mass isotopomer distribution analysis: Bile-salt flux promotes secretion of newly synthesized cholesterol into bile.
AUTHOR: Bandsma R.H.J.; Stellaard F.; Vonk R.J.; Nagel G.T.; Neese R.A.; **Hellerstein M.K.**; Kuipers F.
CORPORATE SOURCE: R.H.J. Bandsma, Groningen Institute for Drug Studies, Department of Paediatrics, Academic Hospital Groningen, Hanzeplein 1, 9713 GZ Groningen, Netherlands
SOURCE: Biochemical Journal, (1 Feb 1998) Vol. 329, No. 3, pp. 699-703. .
Refs: 33
ISSN: 0264-6021 CODEN: BIJOAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 1998
Last Updated on STN: 12 Feb 1998

ABSTRACT: To quantify the contribution of newly synthesized cholesterol to total plasma and biliary cholesterol under physiological conditions, unrestrained rats were infused intravenously with [1-13C]acetate (0.6 mmol/h per kg) from 12:00 to 24:00 h, and fractional and absolute cholesterol-synthesis rates were determined by mass isotopomer distribution analysis (MIDA). As bile diversion leads to changes in cholesterol metabolism, rats were equipped with permanent catheters in the bile duct and duodenum, allowing sampling of small amounts of bile from an intact enterohepatic circulation. For comparison, rats with chronic bile diversion were also studied. Fractional synthesis of plasma cholesterol was 10.8 ± 1.7% (mean ± S.D.) after 12 h in rats with intact circulation. Fractional synthesis of biliary cholesterol was significantly higher than that of plasma cholesterol, i.e. 16.5 ± 2.0% ($P < 0.05$) after 12 h. In contrast, no differences between fractional synthesis of cholesterol in plasma and bile were found in bile-diverted animals (31.8 ± 2.1 and 33.1 ± 3.3% respectively after 12 h). The calculated absolute rate of cholesterol biosynthesis increased from 53 ± 10 to 221 ± 19 μmol/day per kg after bile diversion. A comparison of MIDA results with those obtained from balance studies indicated that MIDA does not assess total body synthesis in rats, presumably because of incomplete equilibration of newly synthesized molecules with cholesterol in the plasma compartment. These studies demonstrate that the contribution of newly synthesized cholesterol to biliary cholesterol is higher than to plasma cholesterol under physiological

conditions, probably reflecting bile-salt-induced secretion of newly formed cholesterol by the periportal hepatocytes.

CONTROLLED TERM: Medical Descriptors:
cholesterol synthesis
plasma
bile
cholesterol blood level
cholesterol metabolism
bile duct
duodenum
nonhuman
male
rat
animal experiment
article
priority journal
Drug Descriptors:
*cholesterol: EC, endogenous compound
bile salt
acetic acid
radioisotope

CAS REGISTRY NO.: (cholesterol) 57-88-5; (acetic acid) 127-08-2, 127-09-3, 64-19-7, 71-50-1

L119 ANSWER 17 OF 30 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
DUPLICATE 1

ACCESSION NUMBER: 2005-658312 [67] WPIX
DOC. NO. CPI: C2005-198851 [67]
DOC. NO. NON-CPI: N2005-539414 [67]
TITLE: Evaluating compounds activity on flux rate by pathways as biomarker.of disease, by administering compound and labeled substrate to system, obtaining samples, measuring and comparing flux rates in system exposed/not exposed to compounds
DERWENT CLASS: B04; D16; K08; S03
INVENTOR: **HELLERSTEIN M K**
PATENT ASSIGNEE: (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005081943	A2	20050909	(200567)*	EN	214[30]	A61K000-00
US 20060020440	A1	20060126	(200609)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005081943	A2	WO 2005-US5660	20050222
US 20060020440	A1 Provisional	US 2004-546580P	20040220
US 20060020440	A1 Provisional	US 2004-581028P	20040617
US 20060020440	A1	US 2005-64197	20050222

PRIORITY APPLN. INFO: US 2004-581028P 20040617

US 2004-546580P 20040220
US 2005-64197 20050222

INT. PATENT CLASSIF.:
MAIN: A61K
IPC ORIGINAL: G06G0007-00 [I,C]; G06G0007-00 [I,C]; G06G0007-48 [I,A]; G06G0007-58 [I,A]

BASIC ABSTRACT:

WO 2005081943 A2 UPAB: 20051223

NOVELTY - Evaluating action of compounds on molecular flux rate through critical pathway as authentic biomarker of disease/compound activity, by administering compound and isotope-labeled substrate to living system, obtaining samples from system, measuring and calculating flux rates in system exposed to/not exposed to compounds, comparing flux rates in system administered/not administered with compounds to evaluate action of compounds on flux rates.

DETAILED DESCRIPTION - Evaluating (M1) an action of one or more compounds on a molecular flux rate through a critical pathway as an authentic biomarker of disease or of compound activity, or toxicity, involves:

(a) exposing a living system to the one or more compound;

(b) administering an isotope-labeled substrate to the living system for a period of time sufficient for the isotope labeled substrate to enter into one or more metabolic pathways of interest and thus enter into and label one or more targeted molecule of interest within the one or more metabolic pathways of interest in the living system, where the one or more metabolic pathways of interest are related to one or more toxic effects;

(c) obtaining one or more samples from the living system, where the one or more samples comprise one or more isotope-labeled targeted molecules of interest;

(d) measuring the content, rate of incorporation and/or pattern or rate of change in content and/or pattern of isotope labeling of the one or more targeted molecule or molecules of interest;

(e) calculating molecular flux rates in the one or more metabolic pathways of interest based on the content and/or pattern or rate of change of content and/or pattern of isotopic labeling in the one or more targeted molecule or molecules of interest;

(f) measuring the molecular flux rates in the one or more metabolic pathways of interest according to steps (b)-(e) in one or more living system not exposed or administered to the one or more compounds as provided by step (a); and

(g) comparing the molecular flux rates in the one or more metabolic pathways of interest in the living system administered the one or more compounds to the molecular flux rates in the one or more metabolic pathways of interest in the living system or systems not administered the one or more compounds to evaluate the action of the one or more compounds on the molecular flux rates. INDEPENDENT CLAIMS are also included for:

(1) rights to drugs as identified by (M1);

(2) an information storage device (I) comprising data obtained by (M1);

(3) an isotopically perturbed molecule (II) generated by (M1);

(4) a kit (K1) for determining screening of one or more compounds for actions on molecular flux rates in one or more metabolic pathways potentially related to disease or one or more toxic effects in a subject, comprising one or more isotope-labeled precursors and instructions for its use;

(5) developing (M2) a compound, involves measuring a molecular flux rate through a critical pathway as a biomarker of interest using one or more isotopes, comparing the results of measuring step with a molecular flux rate through a critical pathway of a biomarker of interest in the presence of a compound of interest, and if the compound of interest changes a molecular flux rate of interest, developing the compound; and

(6) monitoring or diagnosing a medical disease or condition, involves administering an isotope-labeled substrate to a living system for a period of

time sufficient for the isotope labeled substrate to enter into one or more metabolic pathways of interest and thus enter into and label one or more targeted molecule of interest within the one or more metabolic pathways of interest in the living system, obtaining one or more samples from the living system, where the one or more sample include one or more isotope labeled targeted molecule of interest, measuring the content rate of incorporation and/or pattern or rate of change in content and/or pattern of isotope labeling of the one or more targeted molecule of interest, and calculating molecular flux rates in the one or more metabolic pathways of interest based on the content and/or pattern or rate of change of content and/or pattern of isotopic labeling in the one or more targeted molecule of interest to monitor or diagnose the medical disease or condition.

USE - (M1) is useful for evaluating an action of one or more compounds on a molecular flux rate through a critical pathway as an authentic biomarker of disease or of compound activity, or toxicity. The one or more animal models of disease are used for evaluating the actions on molecular flux rates in one or more metabolic pathways potentially related to disease in living system. The one or more animal models of disease is chosen from Alzheimer's disease, heart failure, renal disease, diabetic nephropathy, osteoporosis, hepatic fibrosis, cirrhosis, hepatocellular necrosis, pulmonary fibrosis, scleroderma, renal fibrosis, multiple sclerosis, arteriosclerosis, osteoarthritis, rheumatoid arthritis, psoriasis, skin photoaging, skin rashes, breast cancer, prostate cancer, colon cancer, pancreatic cancer, lung cancer, acquired immunodeficiency syndrome, immunedefects, multiple myeloma, chronic lymphocytic leukemia, chronic myelocytic leukemia, diabetes, diabetic complications, insulin resistance, **obesity**, lipodystrophy, muscle wasting, frailty, deconditioning, angiogenesis, hyperlipidemia, infertility, viral or bacterial infections, auto-immune disorders and immune flares. The living system is chosen from prokaryotic cells, eukaryotic cells, cell lines, cell cultures, isolated tissue preparations, rabbits, dogs, mice, rats, guinea pigs, pigs non-human primates and humans, preferably human (all claimed). (M1) is also useful for identifying potential therapeutic uses or toxicities of the compound or combinations of compound, for measuring the molecular flux rates of the biochemical processes for diagnostic, prognostic and therapeutic purposes, for testing the efficacy of a compound or its combination as a biomarker for drug discovery, development and approval (DDA), medical diagnosis and prognosis, and toxicology, treating or diagnosing, monitoring the disease or disorder.

ADVANTAGE - (M1) is capable of revealing the effects of the chemical entity or entities on the biomarkers. (M1) provides informative, and higher level targets of drug action and functional measures of disease activity with powerful utility in DDA and clinical medicine.

DESCRIPTION OF DRAWINGS - The figure is a graph depicting lipolysis and adipose tissue TG synthesis in mice. MANUAL CODE: CPI: B04-B01B; B04-C02; B04-E01; B04-E07; B04-F02;
B04-H01; B04-N04; B11-C08E; B12-K04; B12-K04A; B12-K04E1;
D05-H09; K08-A; K09-B01
EPI: S03-E14A1; S03-G02B9

TECH

BIOTECHNOLOGY - Preferred Method: In (M1), the molecular flux rates in the one or more metabolic pathways of interest are relevant to an underlying molecular pathogenesis, or causation of, one or more diseases. The concurrent measurement of the molecular flux rates from the metabolic pathways of interest is achieved by use of isotopic labeling techniques or radioisotope labeling techniques. The isotope label used is a stable (that is non-radioactive) isotope, e.g., 2H2O. The one or more compound is an already-approved drug, where the already-approved drug is a Federal Food and Drug Administration-approved drug. The already approved drug is selected randomly on the basis of specific biochemical rationale or hypothesis concerning a hypothesized role in the molecular pathogenesis of

one or more diseases. The one or more compounds are a new chemical entity, or a biological factor. The one or more metabolic pathways of interest are measured in response to a specific dose or a range of doses of the one or more compounds. The already-approved drug is screened for actions on multiple biochemical processes concurrently. The already approved drug is chosen from statins, glitazones, COX-2 inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDS), beta-blockers, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, antibiotics, antiviral agents, hypolipidemic agents, antihypertensives, anti-inflammatory agents, antidepressants, anxiolytics, anti-psychotics and other classes of agents. The isotope labeled substrate is chosen from 2H2O, 2H-glucose, 2H-labeled amino acids, 2H-labeled organic molecules, 13C-labeled organic molecules, 13CO2, 15N-labeled organic molecules, 3H2O, 3H-labeled glucose, 3H-labeled amino acids, 3H-labeled organic molecules, 14C-labeled organic molecules and 14CO2, preferably 2H2O. The one or more samples are collected at known times or intervals after administration or contacting the living system to the isotope-labeled substrate and after exposing the living system to the one or more compound. The combinations of compounds are selected randomly on the basis of a specific biochemical rationale or hypothesis concerning a hypothesized role of one or more of the chemical entities in the molecular pathogenesis of the one or more of diseases.

Preferred Molecule: (II) is chosen from protein, lipid, nucleic acid, glycosaminoglycan, proteoglycan, porphyrin and carbohydrate molecules. The molecule is myelin, amyloid-beta, deoxyribonucleic acid, ribonucleic acid, collagen or triglyceride.

Preferred Kit: (K1) further comprises a tool for administration of precursor molecules and instrument for collecting a sample from the subject.

COMPUTING AND CONTROL - Preferred Device: (I) is a printed report. The medium in which the report is printed on is chosen from paper, plastic and microfiche. (I) is a computer disc, where the disc is chosen from a compact disc, digital video disc, optical disc and magnetic disc. (I) is a computer.

L119 ANSWER 18 OF 30 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
DUPLICATE 2

ACCESSION NUMBER: 2004-419753 [39] WPIX
DOC. NO. CPI: C2004-157629 [39]
DOC. NO. NON-CPI: N2004-333176 [39]
TITLE: Determining metabolism of sugar or fatty acids for diagnosis of e.g. diabetes involves administering a composition comprising deuterium labeled sugar or fatty acid and detecting their incorporation into bodily tissues or fluids
DERWENT CLASS: B03; B04; D16; S03; T01
INVENTOR: **HELLERSTEIN M K**
PATENT ASSIGNEE: (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 106

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004042360	A2	20040521	(200439)*	EN	25[6]	G01N000-00
US 20040115131	A1	20040617	(200440)	EN		A61K051-00
AU 2003291731	A1	20040607	(200469)	EN		
EP 1558293	A2	20050803	(200551)	EN		A61K051-00
JP 2006505777	W	20060216	(200614)	JA	29	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004042360 A2		WO 2003-US35107	20031104
US 20040115131 A1	Provisional	US 2002-423964P	20021104
AU 2003291731 A1		AU 2003-291731	20031104
EP 1558293 A2		EP 2003-768624	20031104
US 20040115131 A1		US 2003-701990	20031104
EP 1558293 A2		WO 2003-US35107	20031104
JP 2006505777 W		WO 2003-US35107	20031104
JP 2006505777 W		JP 2004-550465	20031104

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003291731 A1	Based on	WO 2004042360 A
EP 1558293 A2	Based on	WO 2004042360 A
JP 2006505777 W	Based on	WO 2004042360 A

PRIORITY APPLN. INFO: US 2002-423964P 20021104
US 2003-701990 20031104

INT. PATENT CLASSIF.:
MAIN: A61K051-00; G01N
IPC ORIGINAL: A61K0038-28 [I,A]; A61P0003-00 [I,C]; A61P0003-04 [I,A]; A61P0003-08 [I,A]; A61P0003-10 [I,A]; G01N0027-62 [I,A]; G01N0033-50 [I,A]; G01N0033-66 [I,A]

BASIC ABSTRACT:

WO 2004042360 A2 UPAB: 20060121

NOVELTY - Determining (M1) the metabolism of at least one sugar or fatty acid involves:

(a) administering at least one composition comprising at least one 2H-labeled sugar or fatty acid;

(b) obtaining at least one bodily tissues or fluids; and

(c) detecting incorporation of 2H from the labeled sugars and fatty acids into water.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(a) a kit for determining the metabolism of a sugar or fatty acid in an individual comprising at least one labeled sugar and instructions for use of the kit;

(b) an information storage device (including computer disc such as compact disc, digital video disc and magnetic disc or report printed on paper, plastic and microfiche) comprising data obtained by (M1); and

(c) an isotopically perturbed molecule selected from glycogen, glycerol-triglyceride, triglyceride fatty acid, protein and DNA.

USE - The method is used for:

(a) diagnosing and treating insulin resistance or diabetes mellitus, high-fat diet-induced **obesity**, wasting disorders, hypoglycemia and glycogen storage device in e.g. human, rodent, primate, hamster, guinea pig, dog and pig;

(b) for identifying the effect of a drug agent which can be then manufactured for therapeutic use;

(c) for isolating deuterated water molecule (2H2O);

(d) as a surrogate marker for FDA approval of drugs and for the clinical management of patients (claimed).

Also useful for diagnosing cardiovascular disease.

ADVANTAGE - The metabolism determination facilitates clinical management of patients, and subsequently diagnosis of sugar and fats metabolism related diseases. The method combines simplicity of oral glucose tolerance test and fat tolerance test with improved precision, accuracy and metabolic specificity of

deuterium tracing, at high throughput in inexpensive manner.
MANUAL CODE: CPI: B04-B04B1; B04-B04D5; B04-B04G; B04-C02B2; B04-E01; B04-N02; B05-C08; B10-A07; B10-C04E; B11-C07B2; B11-C07B5; B11-C08A; B11-C08D2; B11-C08E2; B12-K04A; D05-H08; D05-H09; D05-H10
EPI: S03-E14H; T01-J08

TECH
PHARMACEUTICALS - Preferred Method: (M1) Additionally involves:
(a) partially purifying (preferably isolating) the water;
(b) measuring 2H incorporation or incorporation ratio into at least one chemical composition;
(c) measuring endogenous glucose production;
(d) measuring the proportion of labeled glucose stored in tissue glycogen relative to the labeled sugar administered;
(e) measuring the proportion or rate of administered 2H-glucose undergoing glycolysis;
(f) calculating new triglyceride and fatty acid synthesis;
(g) calculating the proportion or storage rate of labeled fatty acids stored in tissue relative to labeled fatty acid administered;
(h) calculating the proportion or storage rate of administered labeled fatty acids undergoing fatty acid oxidation;
(i) calculating the rate or amount of DNA synthesis; and
(j) calculating the rate or total amount of incorporation of the 2H into the water and the chemical composition.
In (M1), the water is detected by gas or liquid chromatography/mass spectrometry, gas chromatography-pyrolysis or combustion-isotope ratio/mass spectrometry, cycloidal mass spectrometry, Fourier-transform-isotope ratio (IR)-spectrometry, near IR laser spectroscopy or isotope ratio mass spectrometry; or by detecting one part 2H in 107 parts water.
ORGANIC CHEMISTRY - Preferred Composition: The composition comprises 2H-labeled glucose. The chemical composition is glucose, glycogen, glycerol-triglyceride, triglyceride fatty acid, proteins or DNA.
Preferred Components: The 2H-labeled glucose is (6,6-2H2)glucose, (1-2H1)glucose or (1,2,3,4,5,6-2H7)glucose.
Preferred Kit: The kit additionally comprises chemical compounds for isolating water or composition selected from glucose, glycogen, protein or DNA, a tool for administering labeled glucose and an instrument for collecting a sample from the subject.
BIOLOGY - Preferred Components: The bodily tissues or fluids are blood, urine, saliva, tears, liver, muscle, adipose, intestine, brain or pancreas.

L119 ANSWER 19 OF 30 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-417873 [42] WPIX
DOC. NO. CPI: C2005-128147 [42]
TITLE: High-throughput screening of compounds to detect unanticipated/unintended biological action, comprises administration of isotope-labeled substrate and comparison of metabolic flux rates of living system exposed and not exposed to compounds
DERWENT CLASS: B04; K08
INVENTOR: **HELLERSTEIN M K; HELLERSTEIN M**
PATENT ASSIGNEE: (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 107

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005051434	A1	20050609	(200542)*	EN	96[8]	

US 20050202406 A1 20050915 (200561) EN
EP 1687035 A1 20060809 (200652) EN
AU 2004293106 A1 20050609 (200681) EN

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005051434 A1		WO 2004-US39722	20041124
US 20050202406 A1	Provisional	US 2003-525261P	20031125
US 20050202406 A1		US 2004-997323	20041123
EP 1687035 A1		EP 2004-812281	20041124
EP 1687035 A1		WO 2004-US39722	20041124
AU 2004293106 A1		AU 2004-293106	20041124

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1687035	A1	Based on	WO 2005051434	A
AU 2004293106	A1	Based on	WO 2005051434	A

PRIORITY APPLN. INFO: US 2003-525261P 20031125
US 2004-997323 20041123
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0049-00 [I,A]; A61K0049-00 [I,C]
IPC RECLASSIF.: A61K0049-00 [I,A]; A61K0049-00 [I,C]; C12Q0001-00 [I,A]; C12Q0001-00 [I,C]; C12Q0001-68 [I,A]; C12Q0001-68 [I,C]; G01N0033-48 [I,A]; G01N0033-48 [I,C]; G01N0033-50 [I,A]; G01N0033-50 [I,C]; G06F0019-00 [I,A]; G06F0019-00 [I,C]

BASIC ABSTRACT:

WO 2005051434 A1 UPAB: 20051222

NOVELTY - High-throughput screening (M1) of compounds (I) for actions on molecular flux rates in metabolic pathways, comprising exposing compounds to a living system; administering an isotope-labeled substrate; measuring the content, rate of incorporation and/or pattern or rate of change in content and/or pattern of isotope labeling of targeted molecules; and comparing molecular flux rates in living systems administered or not administered with the compounds, is new.

DETAILED DESCRIPTION - High-throughput screening (M1) of one or more compounds (I) for actions on molecular flux rates in one or more metabolic pathways, comprises:

(a) exposing (I) to a living system; administering an isotope-labeled substrate to the living system;

(b) administering an isotope-labeled substance to the living system for a time sufficient for the isotope-labeled substrate to enter into and pass through a metabolic pathway of interest and enter into and label a targeted molecule or molecules of interest within the metabolic pathways;

(c) obtaining one or more samples (comprising one or more isotope-labeled targeted molecules of interest) from the living system;

(d) measuring the content, rate of incorporation and/or pattern or rate of change in content and/or pattern of isotope labeling of the targeted molecule or molecules of interest;

(e) calculating molecular flux rates in the metabolic pathways of interest;

(f) measuring the molecular flux rates in the metabolic pathways of interest in a living system not administered with (I); and

(g) comparing the molecular flux rates in the metabolic pathways of interest in the living system administered with (I) to the molecular flux

rates in the metabolic pathways in the living system not administered with (I).

INDEPENDENT CLAIMS are also included for:

(1) the identified compounds;

(2) an information storage device comprising the data;

(3) an isolated isotopically-perturbed molecule generated by the method;

(4) a kit for determining high-throughput screening of (I) for actions on molecular flux rates in one or more metabolic pathways potentially related to disease, comprising: one or more isotope-labeled precursors, and instructions for use of the kit; and

(5) determining whether (I) alters the metabolic flux rate of one or more metabolic pathways, comprising:

(a) treating a living system with (I);

(b) administering an isotope-labeled substrate to the living system for the isotope-labeled substrate to enter into and pass through a metabolic pathway of interest and enter into and label a targeted molecule or molecules of interest within the metabolic pathways in the living system;

(c) obtaining one or more samples from the living system, where the samples comprise one or more isotope-labeled targeted molecules of interest;

(d) measuring the content, rate of incorporation and/or pattern or rate of change in content and/or pattern of isotope labeling of the targeted molecule or molecules of interest;

(e) calculating molecular flux rates in the metabolic pathways of interest; measuring the molecular flux rates in the metabolic pathways of interest in a living system not administered with (I); and

(f) comparing the molecular flux rates in the metabolic pathways of interest in the living system administered with (I) to the molecular flux rates in the metabolic pathways in the living system not administered with (I) to determine whether (I) alters the metabolic flux rate.

USE - The method is useful for high-throughput screening of one or more compounds for actions on molecular flux rates in one or more metabolic pathways. The method allows screening, detection and confirmation of new indications for approved drugs. (All claimed).

ADVANTAGE - The molecular flux rates of the metabolic pathways of two or more diseases are measured concurrently (claimed). The compounds are systematically screened to detect unanticipated or unintended biological actions.

MANUAL CODE: CPI: B04-B01B; B04-E01; B04-F01; B04-N02; B04-N04; B05-C08; B06-D18; B10-A17; B10-G02; B11-C07B5; B11-C08E2; B11-C09; B11-C10A; B11-C11; B12-K04E1; B14-A02; B14-C01; B14-C03; B14-D01B; B14-D01C; B14-E12; B14-F02B; B14-F06; B14-H01; B14-J01A1; B14-J01B; B14-J02D2; B14-J07; B14-N11; K08-X; K09-B02

TECH

PHARMACEUTICALS - Preferred Method: In (M1), the molecular flux rates in the metabolic pathways of interest being measured are relevant to an underlying molecular pathogenesis, or causation of, one or more diseases. The molecular flux rates in the metabolic pathways of interest contribute to the initiation, progression, severity, pathology, aggressiveness, grade, activity, disability, mortality, morbidity, disease sub-classification or other underlying pathogenic or pathologic feature of the disease of interest. The molecular flux rates in the metabolic pathways of interest particularly contribute to the prognosis, survival, morbidity, mortality, stage, therapeutic response, symptomology, disability or other clinical factor of the disease of interest. The concurrent measurement of the molecular flux rates from the metabolic pathways of interest is achieved by use of stable isotopic labeling techniques. The isotope label used is a stable and non-radioactive isotope. The stable isotope used is stable isotope-labeled water (2H2O). The concurrent measurement of the molecular flux rates from the metabolic

pathways of interest is achieved by use of radioisotope labeling techniques. One or more animal models of disease are used for evaluating secondary therapeutic indications. The animal model of disease is: Alzheimer's disease, heart failure, renal disease, diabetic nephropathy, osteoporosis, hepatic fibrosis, cirrhosis, hepatocellular necrosis, pulmonary fibrosis, scleroderma, renal fibrosis, multiple sclerosis, arteriosclerosis, osteoarthritis, rheumatoid arthritis, psoriasis, skin photoaging, skin rashes, breast cancer, prostate cancer, colon cancer, pancreatic cancer, lung cancer, acquired immunodeficiency syndrome, immune defects, multiple myeloma, chronic lymphocytic leukemia, chronic myelocytic leukemia, diabetes, diabetic complications, insulin resistance, **obesity**, lipodystrophy, metabolic syndrome, muscle wasting, frailty, deconditioning, angiogenesis, hyperlipidemia, infertility, viral or bacterial infections, auto-immune disorders or immune flares. The molecular flux rates in the metabolic pathways of interest related to the secondary therapeutic indications are measured in response to a specific dose or a range of doses of (I). The metabolic pathways are: hepatocyte proliferation and destruction, renal tubular cell turnover, lymphocyte turnover, spermatocyte turnover, protein synthesis and breakdown in muscle and heart, liver collagen synthesis and breakdown, myelin synthesis and breakdown in brain or peripheral nerves, breast epithelial cell proliferation, colon epithelial cell proliferation, prostate epithelial cell proliferation, ovarian epithelial cell proliferation, endometrial cell proliferation, bronchial epithelial cell proliferation, pancreatic epithelial cell proliferation, keratin synthesis in skin, keratinocyte proliferation, carbohydrate metabolism, immunoglobulin synthesis, synthesis and breakdown of mitochondrial DNA, synthesis and breakdown of mitochondrial phospholipids, synthesis and breakdown of mitochondrial proteins, synthesis and breakdown of adipose lipids and/or synthesis and breakdown of adipose cells. The action on molecular flux rates in one or more metabolic pathways of interest comprises unintended, unexpected, or unanticipated actions comprising one or more secondary therapeutic indications for (I). The unanticipated or unintended action comprises at least one toxic effect of (I), comprising at least one endorgan toxicity. Preferred Compounds: (I) comprises one or more known drug agents that are federal food and drug administration-approved drug agents, where the drug agents are selected randomly on the basis of a specific biochemical rationale or hypothesis concerning a hypothesized role in the molecular pathogenesis of one or more diseases. (I) comprises one or more new chemical entities, or one or more biological factors. The approved drug agents are: statins, glitazones, cyclooxygenase-2 inhibitors, non-steroidal antiinflammatory drugs, beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors, antibiotics, antiviral agents, hypolipidemic agents, antihypertensives, antiinflammatory agents, antidepressants, anxiolytics, anti-psychotics, sedatives, analgesics, antihistamines, oral hypoglycemic agents, antispasmodics, antineoplastics, cancer chemotherapeutic agents, sex steroids, pituitary hormones, cytokines, chemokines, appetite suppressant agents, thyromimetics, anti-seizure agents, sympathomimetics, sulfa drugs, biguanides or other classes of agents. The molecular flux rates of the metabolic pathways of interest related to the end-organ toxicity are measured in response to a specific dose or a range of doses of (I). The living system is: prokaryotic cells, eukaryotic cells, cell lines, cell cultures, isolated tissue preparations, rabbits, dogs, mice, rats, guinea pigs, pigs, non-human primates or humans (preferably humans). The isotope-labeled substrate is: 2H2O, H218O, 2H-glucose, 2H-labeled amino acids, 2H-labeled organic molecules, 13C-labeled organic molecules, 13CO2, 15N-labeled organic molecules, 3H2O, 3H-labeled glucose, 3H-labeled amino acids, 3H-labeled organic molecules, 14C-labeled organic molecules or 14CO2 (preferably 2H2O). (I) are administered according to established or

hypothesized dose ranges that have the potential for biological activity in the living system. The samples are collected at known times or intervals after administration or contacting the living system to the isotope-labeled substrate and after exposing the living system to (I). The combinations of two or more compounds are exposed to the living system; where synergistic, complementary or antagonistic actions of combinations of compounds on molecular flux rates through the metabolic pathway of interest are determined by comparing the molecular flux rates in the living systems exposed to the combination of compounds to the molecular flux rates in the living systems exposed to a single compound alone or not exposed to any of the compounds being tested. The combinations of compounds are selected randomly on the basis of a specific biochemical rationale or hypothesis concerning a hypothesized role of (I) in the molecular pathogenesis of one or more of the diseases. The unanticipated or unintended actions identified for (I) is developed for approval as a potential new medical indication for (I). The method further comprises the manufacture of drugs at least partially identified by the method. The approved drug agents are screened for actions on multiple biochemical processes concurrently.

Preferred Molecule: The isolated isotopically-perturbed molecule is: protein, lipid; nucleic acid, glycosaminoglycan, proteoglycan, porphyrin or carbohydrate (preferably myelin, amyloid-beta, deoxyribonucleic acid, ribonucleic acid, collagen or triglyceride).

INSTRUMENTATION AND TESTING - Preferred Components: The device is a printed report, where the medium in which the report is printed on is: paper, plastic or microfiche. The device is a computer disc (a compact disc, a digital video disc or a magnetic disc) or a computer.

Preferred Kit: The kit further comprises a tool for administration of precursor molecules, and an instrument for collecting a sample from the subject.

L119 ANSWER 20 OF 30 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-142887 [14] WPIX
DOC. NO. CPI: C2004-057490 [14]
DOC. NO. NON-CPI: N2004-113930 [14]
TITLE: Determination of energy expenditure. useful for identifying a pharmacologic agent having a thermogenic action involves determination of dilution rate of a label water followed by calculation of production rate of metabolic water
DERWENT CLASS: B04; K08; S03
INVENTOR: **HELLERSTEIN M K**
PATENT ASSIGNEE: (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 101

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004003493	A2	20040108	(200414)*	EN	38[5]	G01J000-00
AU 2003253702	A1	20040119	(200447)	EN		
AU 2003253702	A8	20051103	(200629)	EN		A61K049-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004003493	A2	WO 2003-US20052	20030625
AU 2003253702	A1	AU 2003-253702	20030625
AU 2003253702	A8	AU 2003-253702	20030625

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003253702	A1	Based on	WO 2004003493	A
AU 2003253702	A8	Based on	WO 2004003493	A

PRIORITY APPLN. INFO: US 2002-392072P 20020626
INT. PATENT CLASSIF.:
MAIN: A61K049-00; G01J
BASIC ABSTRACT:
WO 2004003493 A2 UPAB: 20050528

NOVELTY - Determination (M1) of energy expenditure involves measuring isotopic content of water in a biological sample and determining total dilution rate of a label in total body water followed by calculating the production rate of metabolic water.

DETAILED DESCRIPTION - Determination (M1) of energy expenditure involves:

(a) either administration of labeled exogenous water for a time to reach a steady-state isotopic content in the individual; or incubation of at least one cell in vitro in a medium containing a known isotopic content of labeled water;

(b) obtaining a biological sample from an individual or from medium;

(c) measuring the isotopic content of water in the biological sample;

(d) comparing the isotopic content of water in the biological sample to the isotopic content in the labeled exogenous water administered to the individual in step (A) to determine the total dilution rate of the label in total body water; and

(e) calculating the production rate of metabolic water from the total dilution rate to determine the energy expenditure in the individual.

INDEPENDENT CLAIMS are also included for the following:

(1) identifying (M2) a pharmacologic agent having a thermogenic action involving:

(a) determining the energy expenditure in an individual or at least one cells prior to exposure to the agent;

(b) exposing the individual or at least one cells to the pharmacologic agent;

(c) determining the energy expenditure in the individual or at least one cells after exposure the pharmacologic agent; and

(d) determining the energy expenditure in the individual or at least one cells before and after exposure to the agent, in which an increase in energy expenditure after exposure to the pharmacologic agent identifies the pharmacologic agent as having a thermogenic action;

(2) identifying (M3) at least one gene involved in a thermogenic action in an individual involving:

(a) determining the energy expenditure in an individual (including transgenic mouse or knockout mouse) or at least one cell, where both have been genetically manipulated or genetically well-characterized, which is characterized by a gene expression chip or proteome measurements; and

(b) correlating the energy expenditure in the individual with the genetic composition or gene expression of the individual to identify at least one genes involved in a thermogenic action in the individual;

(3) identifying (M4) the presence of negative caloric balance in an individual involving:

(a) determining metabolic water production and 2H2O enrichment of body water in an individual prior to the exposure to an intervention;

(b) subjecting the individual to an intervention;

(c) measuring metabolic water production and 2H2O enrichment of body water after the intervention; and

(d) monitoring 2H2O enrichment of body water relative to drinking water, in which a decline in 2H2O enrichment of body water relative to drinking water is indicative of fat mobilization and identifies a negative whole-body fat and caloric balance;

(4) identifying or monitoring (M5) a disease or disorder involving:

(a) determining the energy expenditure of the individual at a first time point;

(b) determining the energy expenditure of an individual at a second time point; and

(c) identifying the disease or disorder by change in the energy expenditure between the first and second time point;

(5) identifying (M6) a beneficial effect of an exercise regimen involving:

(a) determining the energy expenditure of the individual at a first time point;

(b) subjecting the individual to an exercise regimen;

(c) determining the energy expenditure of an individual at a second time point; and

(d) identifying the beneficial effect of the exercise regimen by change in the energy expenditure between the first and second time point; and

(6) a kit for determining energy expenditure in an individual or cells comprises labeled water and instructions for using the kit.

USE - For determining energy expenditure in an individual (including rat, mouse, other experimental animal or human); for identifying a pharmacologic agent having a thermogenic action; for identifying at least one gene involved in a thermogenic action; for identifying the presence of negative caloric balance in an individual; and for identifying or monitoring a disease or disorder (e.g. diabetes mellitus or **obesity** or other disorder of energy balance) (all claimed).

ADVANTAGE - The method measures the total energy expenditure easily and inexpensively.

MANUAL CODE: CPI: B04-B04B; B04-B04D5; B04-B04G; B04-B04H; B05-C08; B11-C07B2; B11-C07B5; B12-K04A; B12-K04E; K09-B; K09-E
EPI: S03-A02

TECH

INORGANIC CHEMISTRY - Preferred Components: The labeled water is 2H2O, 3H2O or H2O18 (preferably 2H2O). The labeled water is administered orally.
BIOLOGY - Preferred Components: The biological sample is urine, blood, saliva, interstitial fluid, edema fluid, lacrimal fluid, inflammatory exudates, synovial fluid, abscess, emphysema, cerebrospinal fluid, sweat, pulmonary secretions, seminal fluid, feces, bile or intestinal secretions. Preferred Method: In (M1), the isotopic enrichment of in the labeled water is determined by isotope-ratio mass spectrometry, gas chromatography/mass spectrometry (GC/MS), cycloidal/MS or Fourier-Transform Infrared Spectroscopy (FTIR). After step (a) in (M1), administration of water is discontinued and at least two biological samples were obtained from the individual comprising endogenous water. In (M4), the intervention is administration of an agent, the presence of at least one transgene, or participation in an exercise regimen or dietary regimen.
INSTRUMENTATION AND TESTING - Preferred Kit: The kit further comprises instructions for performing energy expenditure calculations; tools for administering label water and tools for obtaining biological samples.

L119 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1309586 HCAPLUS Full-text
DOCUMENT NUMBER: 146:55924
TITLE: Methods for monitoring two dimensions of diabetes

pathogenesis (insulin sensitivity and beta-cell sufficiency) using isotope labeled sugars and uses in diagnosis, disease risk assessment, and drug development

INVENTOR(S): **Hellerstein, Marc K.**
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S. Pat. Appl. Publ., 35pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006280682	A1	20061214	US 2006-451735	20060612
WO 2006135879	A2	20061221	WO 2006-US22915	20060612

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-689612P P 20050610
ED Entered STN: 14 Dec 2006

AB Provided are methods for determining concurrently with a simple, minimally invasive test, the adequacy of pancreatic beta-cell compensation and/or the presence of tissue insulin resistance in a subject human or an exptl. animal. The method for determining pancreatic β-cell sufficiency comprises administering isotope-labeled sugars to a subject, wherein said isotope-labeled sugars are metabolized to labeled and/or unlabeled H2O; measuring the isotopic content of H2O in one or more biol. samples from the subject to determine the fractional amount of isotope-labeled H2O; determining the total amount of H2O in said subject before, during or after the administration of the isotope-labeled sugars; and multiplying the fractional amount of by the total amount of H2O to determine the total amount of isotope-labeled H2O to thereby determine pancreatic β-cell sufficiency. The method for determining insulin resistance in a subject comprises (i) determining β-cell sufficiency by the method above; [ii] measuring the amount of insulin in the biol. samples above; and (iii) dividing the total amount of isotope-labeled H2O determined above by the amount of insulin measured to determine the insulin resistance in said subject. The methods allow for the determination of a subject's or exptl. animal's susceptibility to developing type 2 diabetes mellitus (DM2) or to progression to more advanced forms of DM2. Among other uses, the methods allow for diagnostic classification of subjects for decisions regarding therapeutic interventions, clin. differentiation between type 1 DM and DM2, clin. monitoring of treatments intended to reduce risk of developing DM2 in non-diabetic subjects, clin. monitoring of agents intended to improve existing DM2 and to prevent progression of DM2, clin. development and testing of new compds., candidate agents, or candidate therapies for preventing progression to DM2 or disease progression in existing DM2, and preclin. screening of candidate agents or candidate therapies in exptl. animals to identify and

characterize agents having insulin-sensitizing properties, pancreatic stimulatory or regenerative properties or other desirable actions.

L119 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1352995 HCAPLUS Full-text
DOCUMENT NUMBER: 144:347277
TITLE: Sources of plasma glucose and liver glycogen in fasted ob/ob mice
AUTHOR(S): Turner, S. M.; Linfoot, P. A.; Neese, R. A.; **Hellerstein, M. K.**
CORPORATE SOURCE: KineMed Inc., Emeryville, CA, 94608, USA
SOURCE: Acta Diabetologica (2005), 42(4), 187-193
CODEN: ACDAEZ; ISSN: 0940-5429
PUBLISHER: Springer-Verlag Italia Srl
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Dec 2005
AB Alterations in intrahepatic carbohydrate fluxes in ob/ob mice and the effects of acute leptin administration were studied in vivo by use of a dual-isotope tracer infusion. Metabolic sources of plasma glucose (gluconeogenesis (GNG) and glycogenolysis) and hepatic glycogen (GNG, direct synthesis and pre-existing) were determined in 20-h-fasted mice infused with [2-13C1]glycerol and [U13C6]glucose for 3 h. Total glucose output (TGO) and the rate of appearance (Ra) of plasma glycerol were measured by isotope dilution GNG, the direct pathway of hepatic glycogen synthesis and hepatic triose-phosphate flux were determined by mass isotopomer distribution anal. (MIDA). Serum glucose, insulin, leptin and liver glycogen concns. were also measured. After a 24-h fast, ob/ob mice had 2-fold higher TGO, 2.5-fold elevated liver glycogen content and markedly higher glycogenolytic flux to glucose, absolute GNG and direct glycogen synthesis rates (10-fold increased) compared to the control group. Ob/ob mice also had elevated triose-phosphate flux compared to controls (40 vs. 22 mg/kg lean body mass/min). A model of intrahepatic flux distributions in control and ob/ob mice is presented. In summary, elevated fasting plasma glucose concns. are due to increased TGO in ob/ob mice, which is maintained by both increased GNG and increased glycogenolysis. Furthermore, the ob/ob mice have major alterations in fasting hepatic carbohydrate fluxes into triose-phosphate pools and glycogen. We support the model that actions of leptin on hepatic glucose metabolism require insulin or other factors.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L119 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:10553 HCAPLUS Full-text
DOCUMENT NUMBER: 132:61282
TITLE: Methods for measuring cellular proliferation and destruction rates in vitro and in vivo using isotope labels on DNA
INVENTOR(S): **Hellerstein, Marc K.**
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: U.S., 43 pp., Cont.-in-part of U.S. 5,910,403.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6010846	A	20000104	US 1998-75309	19980508

US 5910403	A	19990608	US 1997-857007	19970515
US 6461806	B1	20021008	US 1999-440596	19991115
US 2003068634	A1	20030410	US 2002-155536	20020524
US 6808875	B2	20041026		
US 2005053992	A1	20050310	US 2004-944154	20040916
US 7022834	B2	20060404		
US 2006008796	A1	20060112	US 2005-185610	20050719
PRIORITY APPLN. INFO.:			US 1997-857007	A2 19970515
			US 1998-75309	A3 19980508
			US 1999-440596	A1 19991115
			US 2002-155536	A1 20020524
			US 2004-944154	A1 20040916

ED Entered STN: 06 Jan 2000

AB The present invention relates to methods for measuring the proliferation and destruction rates of cells by measuring DNA synthesis and/or destruction. In particular, the methods utilize non-radioactive stable isotope labels to endogenously label DNA synthesized through the de novo nucleotide synthesis pathway in a cell. The amount of label incorporated in the DNA is measured as an indication of cellular proliferation. The decay of labeled DNA over time is measured as an indication of cellular destruction. Such methods do not involve radioactivity or potentially toxic metabolites, and are suitable for use both in vitro and in vivo. Therefore, the invention is useful for measuring cellular proliferation or cellular destruction rates in humans for the diagnosis, prevention, or management of a variety of disease conditions in which cellular proliferation or cellular destruction is involved. The invention also provides methods for measuring proliferation or destruction of T cells in a subject infected with human immunodeficiency virus (HIV) and methods of screening an agent for a capacity to induce or inhibit cellular proliferation or destruction. In addition, the invention provides methods for measuring cellular proliferation in a proliferating population which utilize both radioactive isotope labels and stable isotopes to endogenously label DNA through the de novo nucleotide synthesis pathway. T cell proliferation rates in individuals infected with HIV was measured by i.v. infusion of [6,6-2H2]glucose. DNA from CD4+ cells was enzymically hydrolyzed, the hydrolyzate was derivatized with FSTFA to the trimethylsilyl derivs. of deoxyribonucleosides, and the derivs. were analyzed by GC-MS.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L119 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:215290 HCAPLUS Full-text

DOCUMENT NUMBER: 136:216038

TITLE: Effects o nicotinic acid on fatty acid kinetics, fuel selection, and pathways of glucose production in women. [Erratum to document cited in CA133:221946]

AUTHOR(S): Wang, Wei; Basinger, Alice; Neese, Richard A.; Christiansen, Mark; **Hellerstein, Marc K.**

CORPORATE SOURCE: Department of Nutritonal Sciences, University of California, Berkeley, CA, 94720-3104, USA

SOURCE: American Journal of Physiology (2000), 279(5, Pt. 1), E1196
CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 22 Mar 2002

AB The plasma glycerol concns. referred to on E53, column 2, line 5, were incorrectly written as units of mg/dL; the correct units should have been mg/L.

L119 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:539003 HCAPLUS Full-text
DOCUMENT NUMBER: 133:221946
TITLE: Effects of nicotinic acid on fatty acid kinetics, fuel selection, and pathways of glucose production in women
AUTHOR(S): Wang, Wei; Basinger, Alice; Neese, Richard A.; Christiansen, Mark; **Hellerstein, Marc K.**
CORPORATE SOURCE: Department of Nutritional Sciences, University of California, Berkeley, CA, 94720-3104, USA
SOURCE: American Journal of Physiology (2000), 279(1, Pt. 1), E50-E59
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 Aug 2000
AB Chronic nicotinic acid (NA) ingestion effectively lowers blood lipid levels, but adverse effects on glucose metabolism have been reported. The acute and chronic effects of NA on lipolysis and glucose metabolism were studied in 5 healthy normolipidemic women. They were studied in two 4-day hospital stays separated by 1 mo; during this 1-mo period they took increasing doses of NA to reach 2 g/day (500 mg, 4 times daily) by the time of the second hospital stay. In the second study the 500 mg NA dose was given at 08:00. The rates of blood plasma appearance (Ra) of free fatty acids (FFA), glycerol, and glucose were determined by isotope dilution ([1,2,3,4-13C4]palmitate, [2-13C1]glycerol, [U-13C6]glucose). Mass isotopomer distribution anal. was used to measure gluconeogenesis and glycogenolysis. Fasting FFA concns., Ra FFA, and Ra glycerol were not significantly elevated after 1 mo. Acute NA dose induced a decrease followed by a rebound overshoot of FFA, Ra FFA, and Ra glycerol. The whole body fat oxidation fell initially and then increased back to basal levels; endogenous glucose production (EGP) increased in parallel with carbohydrate oxidation and then returned to basal values. The increased EGP was entirely due to increased glycogenolysis, not gluconeogenesis. Thus, chronic effects of NA on FFA metabolism are complex (acute suppression followed by overshoot of Ra FFA and FFA on top of a trend toward basal elevations). Responses after NA were consistent with operation of a glucose-fatty acid cycle in peripheral tissues and the secondary effects on EGP were mediated by changes in glycogenolysis, not gluconeogenesis.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L119 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:674893 HCAPLUS Full-text
DOCUMENT NUMBER: 131:350631
TITLE: Effects of a low-fat, high-carbohydrate diet on VLDL-triglyceride assembly, production, and clearance
AUTHOR(S): Parks, Elizabeth J.; Krauss, Ronald M.; Christiansen, Mark P.; Neese, Richard A.; **Hellerstein, Marc K.**
CORPORATE SOURCE: Department of Food Science and Nutrition, University of Minnesota-Twin Cities, St. Paul, MN, 55108, USA
SOURCE: Journal of Clinical Investigation (1999), 104(8), 1087-1096
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Oct 1999

AB Low-fat/high-carbohydrate (LF/HC) diets commonly elevate blood plasma triglyceride (TG) concns., but the kinetic mechanisms responsible for this effect is uncertain. Humans with normolipidemic (NL) and moderately hypertriglyceridemic (HTG) TG levels were studied using control and LF/HC diets. The very-low-d. lipoprotein (VLDL) particle size and TG transport rates, blood plasma nonesterified fatty acid (NEFA) flux, and sources of fatty acids used in VLDL-TG assembly were determined The LF/HC diet led to 60% elevation in TG, 37% decrease in VLDL-TG clearance, and 18% decrease in whole-body fat oxidation, but no significant change in VLDL-apo B or VLDL-TG secretion rates. Elevations in fasting apo B-48 concns. were observed with the LG/HC diet in HTG subjects. In both groups, the fasting de novo lipogenesis was low regardless of the diet. The NEFA pool contributed the great majority of fatty acids to VLDL-TG in NL subjects on both diets, whereas in HTG subjects the contribution of NEFA was somewhat lower overall and was decreased further in individuals on the LF/HC diet. Between 13 and 29% of VLDL-TG fatty acids remained unaccounted for by the sum of de novo lipogenesis and plasma NEFA input in HTG subjects. Thus, the LF/HC diets decreased the VLDL-TG clearance and did not increase the VLDL-TG secretion or de novo lipogenesis. The sources of fatty acids for assembly of VLDL-TG differ between HTG and NL subjects and are further affected by diet composition The presence of chylomicron remnants in the fasting state on LF/HC diets may contribute to elevated TG levels by competing for VLDL-TG lipolysis and by providing a source of fatty acids for hepatic VLDL-TG synthesis. The assembly, production, and clearance of elevated blood plasma VLDL-TG in response to LF/HC diets differ from those for elevated TG on higher-fat diets.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L119 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:641202 HCAPLUS Full-text
DOCUMENT NUMBER: 131:349980
TITLE: Measurement of T-cell kinetics: recent methodological advances
AUTHOR(S): **Hellerstein, M. K.**
CORPORATE SOURCE: Dept of Nutritional Sciences, University of California, Berkeley, CA, 94720-3104, USA
SOURCE: Immunology Today (1999), 20(10), 438-441
CODEN: IMTOD8; ISSN: 0167-4919
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 08 Oct 1999
AB A review and discussion with 23 refs. Measurement of T-cell proliferation and turnover has been limited by methodol. problems, especially in humans. Here, the theory of cellular proliferation measurements is discussed, including special problems arising from T-cell biol.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L119 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:61218 HCAPLUS Full-text
DOCUMENT NUMBER: 128:202629
TITLE: Measurement of cell proliferation by labeling of DNA with stable isotope-labeled glucose: studies in vitro, in animals, and in humans
AUTHOR(S): Macallan, Derek C.; Fullerton, Catherine A.; Neese, Richard A.; Haddock, Katherine; Park, Sunny S.; **Hellerstein, Marc K.**
CORPORATE SOURCE: Department of Nutritional Sciences, University of California at Berkeley, Berkeley, CA, 94720, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(2), 708-713
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Feb 1998
AB A method for measuring DNA synthesis and, thus, cell proliferation, in vivo is presented. The technique consists of administering [6,6-2H2]Glc or [U-13C]Glc, isolating genomic DNA, hydrolyzing enzymically to free deoxyribonucleosides, and derivatizing for GC-MS anal. of dA or dG isotopic enrichments, or both. Comparison of dA or dG to extracellular Glc enrichment (with a correction for intracellular dilution) reveals the fraction of newly synthesized DNA, by application of the precursor-product relationship. Thus, the technique differs from the widely used [3H]thymidine or BrdUrd techniques in that the de novo nucleotide synthesis pathway, rather than the nucleoside salvage pathway, is used to label DNA; the deoxyribose rather than the base moiety is labeled; purine rather than pyrimidine deoxyribonucleosides are analyzed; and stable isotopes rather than radioisotopes are used. The method is applied here in vitro to the growth of HepG2 and H9 cells in culture; in animals to proliferation of intestinal epithelium, thymus, and liver; and in humans to granulocyte turnover in blood. In all instances, measured cell proliferation kinetics were consistent with expected or independently measured kinetics. The method has several advantages over previously available techniques for measuring cell turnover, involves no radioactivity or potentially toxic metabolites, and is suitable for use in humans. The availability of a reliable and safe method for measuring cell proliferation in humans opens up a number of fundamental questions to direct exptl. testing, including basic problems related to cancer, AIDS, and other pathol. states.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L119 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:238073 HCAPLUS Full-text
DOCUMENT NUMBER: 120:238073
TITLE: Effects of cigarette smoking and its cessation on lipid metabolism and energy expenditure in heavy smokers
AUTHOR(S): **Hellerstein, Marc K.**; Benowitz, Neil L.; Neese, Richard A.; Schwartz, Jean-Marc; Hoh, Rebeccah; Jacob, Peyton, III; Hsieh, James; Faix, Dennis
CORPORATE SOURCE: San Francisco Gen. Hosp., Univ. California, San Francisco, CA, 94110, USA
SOURCE: Journal of Clinical Investigation (1994), 93(1), 265-72
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 14 May 1994
AB The relationship between thermogenic and potentially atherogenic effects of cigarette smoking (CS) and its cessation was investigated. Heavy smokers (n = 7, serum cotinine > 200 ng/mL, > 20 cigarettes/d) were maintained on isoenergetic, constant diets for 2 wk, 1 wk with and 1 wk without CS. Stable isotope infusions with indirect calorimetry were performed on day 7 of each phase, after an overnight fast. CS after overnight abstention increased resting energy expenditure by 5% (not significant vs. non-CS phase; P = 0.18). CS increased the flux of FFA by 77%, flux of glycerol by 82%, and serum FFA concns. by 73% (P < 0.02 for each), but did not significantly affect fat oxidation Hepatic reesterification of FFA increased more than threefold (P < 0.03) and adipocyte recycling increased nonsignificantly (P = 0.10). CS-

induced lipid substrate cycles represented only 15% (estimated 11 kcal/d) of observed changes in energy expenditure. De novo hepatic lipogenesis was low (<1-2 g/d) and unaffected by either acute CS or its chronic cessation. Hepatic glucose production was not affected by CS, despite increased serum glycerol and FFA fluxes. Cessation of CS caused no rebound effects on basal metabolic fluxes. In conclusion, a metabolic mechanism for the atherogenic effects of CS on serum lipids (increased hepatic reesterification of FFA) has been documented. Increased entry of FFA accounts for CS-induced increases in serum FFA concns. The thermogenic effect of CS is small or absent in heavy smokers while the potentially atherogenic effect is maintained, and cessation of CS does not induce a rebound lipogenic milieu that specifically favors accrual of body fat in the absence of increased food intake.

L119 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:51022 HCAPLUS Full-text
DOCUMENT NUMBER: 120:51022
TITLE: The indirect pathway of hepatic glycogen synthesis and reduction of food intake by metabolic inhibitors
AUTHOR(S): **Hellerstein, Marc K.**; Xie, Yuhong
CORPORATE SOURCE: Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Life Sciences (1993), 53(24), 1833-45
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 05 Feb 1994
AB The increasingly recognized role of the indirect pathway (glycolysis followed by hepatic gluconeogenesis) for glucose utilization and glycogen synthesis by the liver led the authors to administer 3-mercaptopicolinate (3MP), an inhibitor of phosphoenolpyruvate-carboxykinase, to assess the role of liver glycogen or hexose-phosphates in the food-intake reducing effects of (-)hydroxy-citrate. Administration of (-)hydroxy-citrate increased hepatic glycogen content in i.v. glucose refed rats. Using the glucuronide probe technique, the mechanism of increased glycogen deposition was shown to be prolongation of indirect pathway (recycled) input. Daily (-)hydroxy-citrate significantly reduced food intake (from 12.0 to 6.4 g/day) and had no chronic effect on hepatic glycogen content in rats trained to a single daily meal (meal-fed). Administration of 3MP completely suppressed hepatic glycogen synthesis (<0.5 mg/g) when given alone or with (-)hydroxy-citrate. Isotopic studies confirmed inhibition of the indirect pathway of UDP-glucose synthesis. 3MP accentuated rather than prevented the (-)hydroxy-citrate reduction in food intake in meal-fed rats (intake 2.7 g/day). When given alone, 3MP also reduced intake (6.1 g/day). Severe hypoglycemia was observed (glucose < 20 mg/dL) in several meal-fed rats given repeated daily doses of 3MP, yet food intake did not occur despite food availability. Neither 3MP nor (-)hydroxy-citrate had any effects when given after the daily meal. The authors conclude that the role of the indirect glycogen synthesis pathway must be considered in any theory of regulation of food intake by hepatic metabolites and that, if the effects of these metabolic inhibitors can be shown not to be toxic or non-specific, neither hepatic glycogen nor hexose-phosphates are involved in the food-intake suppressive effects of (-)hydroxycitrate.

Text Search

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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 17 January 2007 (20070117/ED)


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=> FILE EMBASE
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 FILE COVERS 1974 TO 23 Jan 2007 (20070123/ED)

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FILE LAST UPDATED: 22 Jan 2007  (20070122/ED)

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L87 (         6)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L85 AND L74
L88 (         0)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L85 AND L79
L89 (      3942)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72 AND L77
L90 (         1)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L89 AND L82
L91 (         9)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L89 AND L79
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L93 (         0)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L85 AND L92
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                 L81 OR L86 OR L87 OR L88 OR L90 OR L91 OR L93)


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L122          14 L94 NOT L32

=> FILE MEDLINE
FILE 'MEDLINE' ENTERED AT 14:15:45 ON 23 JAN 2007

 FILE LAST UPDATED: 20 Jan 2007 (20070120/UP). FILE COVERS 1950 TO DATE.

  All regular MEDLINE updates from November 15 to December 16 have been
  added to MEDLINE, along with 2007 Medical Subject Headings (MeSH(R))
  and 2007 tree numbers.

  The annual reload will be available in early 2007.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> D QUE L117
L95 (          4)SEA FILE=REGISTRY ABB=ON  PLU=ON  (10390-17-7/BI OR 18991-62-3/
                 BI OR 50-99-7/BI OR 66034-51-3/BI)
L96              SEL  PLU=ON  L95 1- NAME :      41 TERMS
L97 (     295569)SEA FILE=MEDLINE ABB=ON  PLU=ON  L96
L98 (     295569)SEA FILE=MEDLINE ABB=ON  PLU=ON  L97 OR L95
L99 (         59)SEA FILE=MEDLINE ABB=ON  PLU=ON  DEUTER?(2A)GLUCOSE
L100(    1992458)SEA FILE=MEDLINE ABB=ON  PLU=ON  BODY FLUIDS+NT/CT
L101(      21152)SEA FILE=MEDLINE ABB=ON  PLU=ON  INSULIN RESISTANCE+NT/CT
L102(         28)SEA FILE=MEDLINE ABB=ON  PLU=ON  L99 AND L100
L103(          2)SEA FILE=MEDLINE ABB=ON  PLU=ON  L102 AND L101
L104(          3)SEA FILE=MEDLINE ABB=ON  PLU=ON  L99 AND L101
L105(      12366)SEA FILE=MEDLINE ABB=ON  PLU=ON  GLYCOLYSIS/CT
L106(          6)SEA FILE=MEDLINE ABB=ON  PLU=ON  L99 AND L105
L107(      12470)SEA FILE=MEDLINE ABB=ON  PLU=ON  L98 AND L101
L108(       7044)SEA FILE=MEDLINE ABB=ON  PLU=ON  L107 AND L100
L109(         36)SEA FILE=MEDLINE ABB=ON  PLU=ON  L108 AND L105
L110(      73584)SEA FILE=MEDLINE ABB=ON  PLU=ON  OBESITY+NT/CT
L111(         10)SEA FILE=MEDLINE ABB=ON  PLU=ON  L109 AND L110
L112(         19)SEA FILE=MEDLINE ABB=ON  PLU=ON  (L103 OR L104 OR L106 OR
                 L111)
L113(         14)SEA FILE=MEDLINE ABB=ON  PLU=ON  L112 AND PY<=2003
L114(     390158)SEA FILE=MEDLINE ABB=ON  PLU=ON  FATTY ACIDS+NT/CT
L115(         12)SEA FILE=MEDLINE ABB=ON  PLU=ON  L114 AND L100 AND L101 AND
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L116(         12)SEA FILE=MEDLINE ABB=ON  PLU=ON  L115 AND PY<=2003
L117          23 SEA FILE=MEDLINE ABB=ON  PLU=ON  L113 OR L116


=> S L117 NOT L38
L123          23 L117 NOT L38

=> FILE WPIX
FILE 'WPIX' ENTERED AT 14:16:20 ON 23 JAN 2007
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    http://scientific.thomson.com/dwpi-manualcoderevision <<<
'BI,ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

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L118          7 SEA FILE=WPIX ABB=ON  PLU=ON  DEUTER?/BI,ABEX(5A)GLUCOSE/BI,ABE
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=> S L118 NOT L41
L124          7 L118 NOT L41

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PROCESSING COMPLETED FOR L120
PROCESSING COMPLETED FOR L121
PROCESSING COMPLETED FOR L124
PROCESSING COMPLETED FOR L122
L125         76 DUP REM L123 L120 L121 L124 L122 (11 DUPLICATES REMOVED)
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ANSWERS '1-23' FROM FILE MEDLINE
ANSWERS '24-35' FROM FILE BIOSIS
ANSWERS '36-56' FROM FILE EMBASE
ANSWERS '57-63' FROM FILE WPIX
ANSWERS '64-76' FROM FILE HCAPLUS

=> D IALL 1-56;D IALL ABEQ TECH 57-63;D IBIB ED ABS 64-76

L125 ANSWER 1 OF 76 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002633076 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12391573
TITLE: Measurement of insulin sensitivity indices using 13C-glucose and gas chromatography/combustion/isotope ratio mass spectrometry.
AUTHOR: Clapperton Allan T; Coward W Andrew; Bluck Leslie J C
CORPORATE SOURCE: Medical Research Council Human Nutrition Research, Elsie Widdowson Laboratory, Peterhouse Park, Fulbourn Road, Cambridge CB1 9NL, UK.. allan.clapperton@mrc-hnr.cam.ac.uk
SOURCE: Rapid communications in mass spectrometry : RCM, **(2002)** Vol. 16, No. 21, pp. 2009-14.
Journal code: 8802365. ISSN: 0951-4198.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 23 Oct 2002
Last Updated on STN: 17 Dec 2002
Entered Medline: 3 Dec 2002

ABSTRACT:
Important aspects of glucose metabolism can be quantified by using the minimal model of glucose kinetics to interpret the results of intravenous glucose tolerance tests. The power of this methodology can be greatly increased by the addition of stable isotopically labelled tracer to the glucose bolus dose. This allows the separation of glucose disposal from endogenous glucose production and also increases the precision of the estimates of the physiological parameters measured. Until now the tracer of choice has been ***deuteriated*** **glucose** and the analytical technique has been gas chromatography/mass spectrometry (GC/MS). The consequence of this choice is that nearly 2 g of labelled material are needed and this makes the test expensive. We have investigated the use of (13)C-labelled glucose as the tracer in combination with gas chromatography/combustion/isotope ratio mass spectrometry (GC/C/IRMS) as the analytical technique. This methodology offers superior analytical precision when compared with the conventional method and so the amount of tracer used, and hence the cost, can be reduced considerably. Healthy non-obese male volunteers were recruited for a standard intravenous glucose tolerance test (IVGTT) protocol but 6,6-(2)H-glucose and 1-(13)C-glucose were administered simultaneously. Tracer/tracee ratios were derived from isotope ratio measurements of plasma glucose using both GC/MS and GC/C/IRMS. The results of these determinations indicated that the two tracers behaved identically under the test protocol. The combination of these results with plasma glucose and insulin concentration data allowed determination of the minimal model parameters S*g and S*i. The parameter relating to insulin-assisted glucose disposal, S*i, was found to be the same in the two techniques, but this was not the case for the non-insulin-dependent parameter S*g.

CONTROLLED TERM: Check Tags: Male
Adult
Carbon Isotopes: DU, diagnostic use

Glucose: AD, administration & dosage
*Glucose: AN, analysis
*Glucose: ME, metabolism
Glucose Tolerance Test: EC, economics
Glucose Tolerance Test: MT, methods
Humans
Injections, Intravenous
***Insulin Resistance: PH, physiology**
*Mass Fragmentography: MT, methods
Middle Aged
Tritium: DU, diagnostic use

CAS REGISTRY NO.: 10028-17-8 (Tritium); 50-99-7 (Glucose)
CHEMICAL NAME: 0 (Carbon Isotopes)

L125 ANSWER 2 OF 76 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 95170806 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7866471
TITLE: The effects of weight loss in obese subjects on the thermogenic, metabolic and haemodynamic responses to the glucose clamp.
AUTHOR: Webber J; Donaldson M; Allison S P; Fukagawa N K; Macdonald I A
CORPORATE SOURCE: Department of Physiology and Pharmacology, Queen's Medical Centre, Nottingham, UK.
SOURCE: International journal of obesity and related metabolic disorders : journal of the International Association for the Study of Obesity, **(1994 Nov)** Vol. 18, No. 11, pp. 725-30.
Journal code: 9313169. ISSN: 0307-0565.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 7 Apr 1995
Last Updated on STN: 6 Feb 1998
Entered Medline: 30 Mar 1995

ABSTRACT:
The aim of this work was to examine the effects of weight loss in obese subjects on the thermogenic, metabolic and cardiovascular responses to a glucose clamp. Resting measurements were made, followed by a hyperinsulinaemic (100 mU/m2/min) euglycaemic clamp (4.5 mmol/l). The subjects were six healthy, obese subjects (mean body mass index before weight loss 37.0 +/- 1.7 kg/m2 and after weight loss 31.4 +/- 2.3 kg/m2). The following measurements were made: indirect calorimetry, blood pressure, heart rate, forearm blood flow, plasma catecholamines, plasma **deuterated glucose** turnover before and during a glucose clamp. Glucose disposal during the clamp increased from 2.53 +/- 0.40 to 3.31 +/- 0.42 mmol/min after weight loss ($P < 0.01$). Glucose-induced thermogenesis rose from 0.15 +/- 0.09 to 0.50 +/- 0.12 kJ/min ($P < 0.05$). The apparent cost of glucose storage was not significantly different from zero prior to weight loss, but increased to 11.0 +/- 2.2% after weight loss. In response to the clamp endogenous glucose production was suppressed by 66 +/- 7% initially and this was not affected by weight loss. Weight loss was accompanied by increased peripheral insulin sensitivity and glucose-induced thermogenesis, but it did not affect hepatic insulin sensitivity.

CONTROLLED TERM: Check Tags: Female; Male
Adult
Blood Glucose: AN, analysis
Blood Glucose: ME, metabolism

Blood Pressure: PH, physiology
Body Mass Index
*Body Temperature Regulation: PH, physiology
Calorimetry
Cardiovascular Physiology
Catecholamines: BL, blood
*Energy Metabolism: PH, physiology
Epinephrine: BL, blood
Glucose Clamp Technique
Heart Rate: PH, physiology
*Hemodynamic Processes: PH, physiology
Humans
Insulin: BL, blood
Insulin Resistance: PH, physiology
*Obesity: PP, physiopathology
Research Support, Non-U.S. Gov't
Respiration: PH, physiology
*Weight Loss: PH, physiology

CAS REGISTRY NO.: 11061-68-0 (Insulin); 51-43-4 (Epinephrine)
CHEMICAL NAME: 0 (Blood Glucose); 0 (Catecholamines)

L125 ANSWER 3 OF 76 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 95075270 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7984074
TITLE: Metabolic loss of deuterium from isotopically labeled glucose.
AUTHOR: Ben-Yoseph O; Kingsley P B; Ross B D
CORPORATE SOURCE: Department of Radiology, School of Medicine, University of Michigan Medical Center, Ann Arbor.
CONTRACT NUMBER: P20 NS31114 (NINDS)
P30 CA21765 (NCI)
R29 CA59009 (NCI)
SOURCE: Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine, **(1994 Sep)** Vol. 32, No. 3, pp. 405-9.
Journal code: 8505245. ISSN: 0740-3194.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 16 Jan 1995
Last Updated on STN: 6 Feb 1998
Entered Medline: 3 Jan 1995

ABSTRACT:
The isotopically substituted molecule (6-13C, 1, 6, 6-2H3)glucose was evaluated to determine whether metabolic 2H loss would prevent its use in quantitating pentose phosphate pathway (PPP) activity. PPP activity causes the C1 of glucose to be lost as CO2, while C6 can appear in lactate. 2H NMR analysis of the lactate produced from this glucose can distinguish (3-2H)-lactate (from C1 of glucose) from (3-13C, 3, 3-2H2)lactate (from C6 of glucose). 2H NMR spectroscopic analysis of medium containing (6-13C, 1, 6, 6-2H3)glucose after incubation with cultured rat 9L glioma cells suggested a 30.8 +/- 2.1% PPP activity as compared with 6.0 +/- 0.8% from separate, parallel incubations with (1-13C)glucose and (6-13C)glucose. Subsequent experiments with other isotopically labeled glucose molecules suggest that this discrepancy is due to selective loss of 2H from the C1 position of glucose, catalyzed by phosphomannose isomerase. Failure to consider 2H exchange from the C1 and C6 positions of glucose can lead to incorrect conclusions in metabolic studies

utilizing this and other **deuterated** or tritiated **glucose** molecules.

CONTROLLED TERM: Check Tags: Male
Animals
Brain Neoplasms: EN, enzymology
*Brain Neoplasms: ME, metabolism
Carbon Isotopes
Cerebral Cortex: EN, enzymology
Cerebral Cortex: ME, metabolism
Deuterium: CH, chemistry
*Deuterium: ME, metabolism
Glioma: EN, enzymology
*Glioma: ME, metabolism
Glucose: CH, chemistry
*Glucose: ME, metabolism
Glycolysis
Lactates: CH, chemistry
*Lactates: ME, metabolism
Lactic Acid
*Magnetic Resonance Spectroscopy: DU, diagnostic use
Mannose-6-Phosphate Isomerase: ME, metabolism
Mass Fragmentography
Models, Chemical
*Pentose Phosphate Pathway
Pyruvate Kinase: ME, metabolism
Rats
Rats, Inbred F344
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Tumor Cells, Cultured

CAS REGISTRY NO.: 50-21-5 (Lactic Acid); 50-99-7 (Glucose); 7782-39-0 (Deuterium)

CHEMICAL NAME: 0 (Carbon Isotopes); 0 (Lactates); EC 2.7.1.40 (Pyruvate Kinase); EC 5.3.1.8 (Mannose-6-Phosphate Isomerase)

L125 ANSWER 4 OF 76 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 92289150 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 1817812

TITLE: Variable expression of isotopic discrimination in metabolic flows.

AUTHOR: Malaisse W J; Malaisse-Lagae F; Sener A

CORPORATE SOURCE: Laboratory of Experimental Medicine, Brussels Free University, Belgium.

SOURCE: Diabetes research (Edinburgh, Lothian), **(1991 Jun)** Vol. 17, No. 2, pp. 51-65.
Journal code: 8502339. ISSN: 0265-5985.

PUB. COUNTRY: SCOTLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199207

ENTRY DATE: Entered STN: 24 Jul 1992
Last Updated on STN: 3 Feb 1997
Entered Medline: 16 Jul 1992

ABSTRACT:
Isotopic discrimination in reaction velocity may affect to a variable extent the estimation of metabolic flow when a metabolic intermediate is catabolized by two pathways with different degrees of discrimination. This was explored in erythrocytes exposed to 14C- or 3H-labelled D-glucose in the absence or presence of menadione. In the absence of menadione, when the pentose phosphate

pathway accounted for only 5% of the D-glucose 6-phosphate turnover, the oxidation of C1-protonated or C1-deuterated D-[U-14C]glucose and D-[1-14C]glucose, mixed with the homologous non-radioactive D-[1-1H]glucose or D-[1-2H]glucose, indicated that, relative to the phosphorylation of the hexose, C1- **deuterated D-glucose** was less efficiently converted to 14CO2 than C1-protonated D-glucose. Moreover, in the absence of menadione, non-deuterated D-[U-14C]glucose and D-[1-14C]glucose were more efficiently oxidized in cells exposed to D-[1-2H]glucose rather than D-[1-1H]glucose. In the presence of menadione, which increased more than ten-fold the flow rate through the pentose phosphate pathway, the phenomenon of isotopic discrimination was either revealed or masked. These data indicate that the phenomenon of isotopic discrimination may indeed affect to a variable extent the estimation of a given metabolic flow.

CONTROLLED TERM: Animals
*Blood Glucose: ME, metabolism
Carbon Dioxide: AN, analysis
Carbon Dioxide: BL, blood
Carbon Radioisotopes
Citric Acid Cycle
Deuterium
Erythrocytes: DE, drug effects
*Erythrocytes: ME, metabolism
Glucose-6-Phosphate
Glucosephosphates: BL, blood
***Glycolysis**
Humans
In Vitro
Kinetics
Pentose Phosphate Pathway
*Radioisotope Dilution Technique
Rats
Research Support, Non-U.S. Gov't
Tritium
Vitamin K: PD, pharmacology

CAS REGISTRY NO.: 10028-17-8 (Tritium); 12001-79-5 (Vitamin K); 124-38-9 (Carbon Dioxide); 56-73-5 (Glucose-6-Phosphate); 7782-39-0 (Deuterium)

CHEMICAL NAME: 0 (Blood Glucose); 0 (Carbon Radioisotopes); 0 (Glucosephosphates)

L125 ANSWER 5 OF 76 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 88312894 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 3409997

TITLE: Dynamic monitoring of corneal carbohydrate metabolism using high-resolution deuterium NMR spectroscopy.

AUTHOR: Aguayo J B; McLennan I J; Graham C Jr; Cheng H M

CORPORATE SOURCE: Howe Laboratory of Ophathalmology, Harvard Medical School, Boston, MA 02114.

CONTRACT NUMBER: EY07620 (NEI)

SOURCE: Experimental eye research, **(1988 Aug)** Vol. 47, No. 2, pp. 337-43.
Journal code: 0370707. ISSN: 0014-4835.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198810

ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 8 Mar 1990
Entered Medline: 13 Oct 1988

ABSTRACT:
Glucose metabolism in rabbit corneas was monitored with deuterium (D or 2H) NMR spectroscopy. The corneas were incubated in 5.5 mM **deuterated** ***glucose*** (**glucose**-6, 6-D2). A 2.5 micrograms change in lactate and a 4.1 micrograms change in glucose could be detected by the NMR method. The mean rates of glucose utilization and lactate production in intact rabbit corneas were 248- and 151 micrograms h-1, respectively. The lactate production/glucose utilization ratio of 0.60, i.e. 60% of total glucose is metabolized to lactate, confirms that glycolysis is the principal pathway for glucose catabolism. Further, based on enrichment of the HDO signal (which refers to the naturally abundant deuterium signal arising from ***deuterons*** in water), **glucose** oxidation through Krebs cycle and its associated pathways is estimated to be 90 micrograms h-1 or 36% of total consumption. The significant advantages of deuterium NMR spectroscopy over other NMR techniques (e.g. 13C spectroscopy) are: (1) shorter acquisition times because of the short relaxation times of deuterated metabolites; (2) the HDO signal can be used as the internal reference; and (3) significant reduction in cost and high availability of 2H-labeled compounds. Deuterium NMR spectroscopy is therefore a reliable and effective means with which the corneal glycolytic activity prior to transplantation can be readily assessed.

CONTROLLED TERM: Animals
*Cornea: ME, metabolism
Deuterium
*Glucose: ME, metabolism
Glycolysis
Lactates: ME, metabolism
Magnetic Resonance Spectroscopy
Rabbits
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Time Factors

CAS REGISTRY NO.: 50-99-7 (Glucose); 7782-39-0 (Deuterium)
CHEMICAL NAME: 0 (Lactates)

L125 ANSWER 6 OF 76 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 85289922 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 4031071
TITLE: Substrate cycling between gluconeogenesis and glycolysis in euthyroid, hypothyroid, and hyperthyroid man.
AUTHOR: Shulman G I; Ladenson P W; Wolfe M H; Ridgway E C; Wolfe R R
CONTRACT NUMBER: AM-16791 (NIADDK)
RR-00073 (NCRR)
RR-1066 (NCRR)
+
SOURCE: The Journal of clinical investigation, **(1985 Aug)** Vol. 76, No. 2, pp. 757-64.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198510
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 2 Oct 1985

ABSTRACT:
Substrate, or futile cycles, have been hypothesized to be under hormonal control, and important in metabolic regulation and thermogenesis. To define the role of thyroid hormones in the regulation of substrate cycling in

glycolysis and gluconeogenesis, we measured rates of cycling in normal (n = 4), hypothyroid (n = 5), and hyperthyroid (n = 5) subjects employing a stable isotope turnover technique. **Glucose** labeled with **deuterium** at different positions (2-D1-, 3-D1-, and 6,6-D2-glucose) was given as a primed-constant infusion in tracer doses, and arterialized plasma samples were obtained and analyzed by gas-chromatography mass-spectrometry for the steady state enrichment of glucose that was labeled at the various positions. The rate of appearance (Ra) was then calculated for each isotopic tracer. The difference between the Ra determined by 2-D1-glucose (Ra2) and the Ra determined by 3-D1-glucose (Ra3) represents the substrate cycling rate (SCR) between glucose and glucose-6-phosphate. The difference between the Ra determined by 3-D1-glucose (Ra3) and the Ra determined by 6,6-D2-glucose (Ra6) represents the SCR between fructose-6-phosphate and fructose-1,6-diphosphate. The difference between Ra2 and Ra6 represents the combined SCR of both cycles. In normal subjects (serum thyroxine [T4] = 8.4 +/- 1.2 microgram/dl (all expressions, mean +/- SD), n = 4), the rates of appearance for Ra2, Ra3, and Ra6 were 3.23 +/- 0.56, 2.64 +/- 0.50, and 2.00 +/- 0.27 mg/kg X min, respectively, whereas those in the hypothyroid subjects (T4 = 1.0 +/- 0.8 microgram/dl; n = 5) were 1.77 +/- 0.56 (P less than 0.01), 1.52, 1.57 +/- 0.31 (P less than 0.05) mg/kg X min, respectively. Conversely, the rates of appearance for Ra2 and Ra6 in the hyperthyroid subjects (T4 = 23.9 +/- 3.6 micrograms/dl) were 3.94 +/- 0.43 (P less than 0.05) and 2.54 +/- 0.22 (P less than 0.02), respectively, compared with the normal subjects. On the basis of these data, we noted that the normal subjects had a combined SCR of 1.23 +/- 0.35 mg/kg X min. In contrast, the hypothyroid patients had a significantly decreased combined SCR, 0.20 +/- 0.54 mg/kg X min (P less than 0.02). The hyperthyroid patients had a combined SCR of 1.39 +/- 0.23 mg/kg X min (P less than NS). To determine whether these cycles responded to thyroid hormone treatment, these same hypothyroid subjects were acutely treated for 1 wk with parenteral 50 micrograms/d sodium L-triiodothyronine and chronically with 100-150 micrograms/d L-thyroxine. After 7 d, their mean oxygen consumption rate and carbon dioxide production rate increased significantly from 102+/-13 micromol/kg.min, to 147+/-34 micromol/kg.min (P<0.05), and from 76+/-13 micromol/kg.min to 111+/-19 micromol/kg.min (P<0.05), respectively. The combined SCR (Ra(2)--Ra(6) remained unchanged at 0.07+/-0.37 mg/kg.min. However, after 6 mo of oral L-thyroxine therapy (T(4)=9.5+/-1.4 microgram/kl) the treated hypothyroid patients had increased their combined SCR (Ra(2)--Ra(6)) to 0.86 +/-0.23 mg/kg.min (P<0.02), a value not significantly different from the combined SCR of normal subjects. We conclude that substrate cycling between glucose and glucose-6-phosphate and between fructose-6-phosphate and fructose-1,6-diphosphate occurs in man and is affected by thyroid hormone. Substrate cycles may represent a mechanism by which thyroid hormone alters the sensitivity of certain reactions to metabolic signals.

CONTROLLED TERM: Check Tags: Female; Male
Adult
*Gluconeogenesis
***Glycolysis**
Humans
Hyperthyroidism: DT, drug therapy
*Hyperthyroidism: ME, metabolism
Hypothyroidism: DT, drug therapy
*Hypothyroidism: ME, metabolism
Mass Fragmentography
Middle Aged
Models, Biological
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Thyroxine: TU, therapeutic use
Time Factors

Triiodothyronine: TU, therapeutic use
CAS REGISTRY NO.: 6893-02-3 (Triiodothyronine); 7488-70-2 (Thyroxine)

L125 ANSWER 7 OF 76 MEDLINE on STN
ACCESSION NUMBER: 2003112829 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12488242
TITLE: Effect of weight loss on muscle lipid content in morbidly obese subjects.
AUTHOR: Gray Robert E; Tanner Charles J; Pories Walter J; MacDonald Kenneth G; Houmard Joseph A
CORPORATE SOURCE: Department of Exercise and Sport Science, East Carolina University, Greenville, North Carolina 27858, USA.
CONTRACT NUMBER: DK-56112 (NIDDK)
SOURCE: American journal of physiology. Endocrinology and metabolism, **(2003 Apr)** Vol. 284, No. 4, pp. E726-32. Electronic Publication: 2002-12-17.
Journal code: 100901226. ISSN: 0193-1849.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 11 Mar 2003
Last Updated on STN: 16 Apr 2003
Entered Medline: 10 Apr 2003

ABSTRACT:
The purpose of this study was to test the hypothesis that weight loss results in a reduction in intramuscular lipid (IMCL) content that is concomitant with enhanced insulin action. Muscle biopsies were obtained from morbidly obese individuals [body mass index (BMI) 52.2 +/- 2.5 kg/m(2); n = 6] before and after gastric bypass surgery, an intervention that improves insulin action. With intervention, there was a 47% reduction ($P < 0.01$) in BMI and a 93% decrease in homeostasis model assessment, or HOMA (7.0 +/- 1.9 vs. 0.5 +/- 0.1). Histochemically determined IMCL content decreased ($P < 0.05$) by approximately 30%. In relation to fiber type, IMCL was significantly higher in type I vs. type II fibers. In both fiber types, there were reductions in IMCL and trends for muscle atrophy. Despite these two negating factors, the IMCL-to-fiber area ratio still decreased by approximately 44% with weight loss. In conclusion, despite differing initial levels and possible atrophy, weight loss appears to decrease IMCL deposition to a similar relative extent in type I and II muscle fibers. This reduction in intramuscular triglyceride may contribute to enhanced insulin action seen with weight loss.

CONTROLLED TERM: Check Tags: Female; Male
Adipose Tissue: ME, metabolism
Adult
Blood Glucose: ME, metabolism
Glycolysis
Humans
Insulin: BL, blood
Insulin Resistance
*Lipid Metabolism
Muscle Fibers, Fast-Twitch: ME, metabolism
Muscle Fibers, Slow-Twitch: ME, metabolism
Muscle, Skeletal: CY, cytology
*Muscle, Skeletal: ME, metabolism
***Obesity, Morbid: ME, metabolism**
Oxidation-Reduction
Research Support, U.S. Gov't, P.H.S.
*Weight Loss: PH, physiology
CAS REGISTRY NO.: 11061-68-0 (Insulin)

CHEMICAL NAME: 0 (Blood **Glucose**)

L125 ANSWER 8 OF 76 MEDLINE on STN
ACCESSION NUMBER: 2001094556 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11120655
TITLE: Gluconeogenesis in moderately and severely hyperglycemic patients with type 2 diabetes mellitus.
AUTHOR: Boden G; Chen X; Stein T P
CORPORATE SOURCE: Division of Endocrinology/Diabetes/Metabolism, Temple University Hospital, Philadelphia, Pennsylvania 19140, USA.. bodengh@tuhs.temple.edu
CONTRACT NUMBER: R01-AA-10221 (NIAAA)
R01-AG-07988 (NIA)
R01-AG-14098 (NIA)
+
SOURCE: American journal of physiology. Endocrinology and metabolism, **(2001 Jan)** Vol. 280, No. 1, pp. E23-30.
Journal code: 100901226. ISSN: 0193-1849.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 25 Jan 2001

ABSTRACT:
We tested the generally accepted concept that increased gluconeogenesis (GNG) and endogenous glucose production (EGP) are the main reasons for postabsorptive hyperglycemia in patients with type 2 diabetes mellitus (T2DM). GNG was measured with the (2)H(2)O method by use of both the C5-to-C2 ratio (C5/C2, with gas chromatography-mass spectrometry) and the C5-to-(2)H(2)O ratio (C5/(2)H(2)O, with isotope ratio mass spectrometry), and EGP was measured with 3-[(3)H]glucose in 27 patients with T2DM [13 with fasting plasma glucose (FPG) >10 mM and 14 with FPG <10 mM] and in 7 weight- and age-matched nondiabetic controls. The results showed 1) that GNG could be determined accurately with (2)H(2)O by using either C5/C2 or C5/(2)H(2)O; 2) that whereas after an overnight fast of 16 h, GNG was higher in the entire group of patients with T2DM than in controls (6.4 vs. 5.0 micromol. kg(-1). min(-1) or 60.4 vs. 51.4% of EGP, $P < 0.02$), GNG was within normal limits (less than the mean +/- 2 SD of controls or <65.3%) in 11/14 (79%) patients with mild to moderate hyperglycemia (FPG <10 mM) and in 5/13 (38%) of patients with severe hyperglycemia (FPG 10-20 mM); 3) that elevated GNG in T2DM was associated with a 43% decrease in prehepatic insulin secretion, i.e., with hepatic insulin deficiency; and 4) that FPG correlated significantly with glucose clearance (insulin resistance) ($r = 0.70$) and with GNG ($r = 0.50$) or EGP ($r = 0.45$). We conclude 1) that peripheral insulin resistance is at least as important as GNG (and EGP) as a cause of postabsorptive hyperglycemia in T2DM and 2) that GNG and EGP in T2DM are increased under conditions of significant hepatic insulin deficiency and thus probably represent a late event in the course of T2DM.

CONTROLLED TERM: Check Tags: Female; Male
Aged
Blood Glucose: BI, biosynthesis
Deuterium
*Diabetes Mellitus, Type 2: ME, metabolism
Fasting: PH, physiology
Fatty Acids, Nonesterified: BL, blood
Glucagon: BL, blood

*Gluconeogenesis: PH, physiology
Glucose: PK, pharmacokinetics
Glycolysis: PH, physiology
Human Growth Hormone: BL, blood
Humans
Hydrocortisone: BL, blood
*Hyperglycemia: ME, metabolism
Insulin: ME, metabolism
Insulin: SE, secretion
Insulin Resistance: PH, physiology
Ketone Bodies: BL, blood
Middle Aged
Research Support, U.S. Gov't, P.H.S.
Tritium: DU, diagnostic use

CAS REGISTRY NO.: 10028-17-8 (Tritium); 11061-68-0 (Insulin); 12629-01-5 (Human Growth Hormone); 50-23-7 (Hydrocortisone); 50-99-7 (Glucose); 7782-39-0 (Deuterium); 9007-92-5 (Glucagon)

CHEMICAL NAME: 0 (Blood Glucose); 0 (Fatty Acids, Nonesterified); 0 (Ketone Bodies)

L125 ANSWER 9 OF 76 MEDLINE on STN

ACCESSION NUMBER: 1999447251 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10516135

TITLE: Acute effect of growth hormone to induce peripheral insulin resistance is independent of FFA and insulin levels in rats.

AUTHOR: Kim J K; Choi C S; Youn J H

CORPORATE SOURCE: Department of Physiology, University of Southern California School of Medicine, Los Angeles, California 90089-9142, USA.

CONTRACT NUMBER: R-29-DK-47947 (NIDDK)

SOURCE: The American journal of physiology, **(1999 Oct)** Vol. 277, No. 4 Pt 1, pp. E742-9.
Journal code: 0370511. ISSN: 0002-9513.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199911

ENTRY DATE: Entered STN: 11 Jan 2000
Last Updated on STN: 10 Dec 2002
Entered Medline: 22 Nov 1999

ABSTRACT:
To examine whether growth hormone (GH) induces peripheral insulin resistance by altering plasma free fatty acid (FFA) or insulin levels, the effects of GH infusion on insulin-stimulated glucose fluxes were studied in conscious rats under two protocols. In study 1, either saline (n = 7) or human recombinant GH (21 microg. kg(-1). h(-1); n = 8) was infused for 300 min, and insulin-stimulated glucose fluxes were estimated during the final 150-min period of hyperinsulinemic euglycemic clamps. In study 2, hyperinsulinemic euglycemic clamps were first conducted for 150 min (to raise plasma insulin and suppress FFA levels), and saline or GH (n = 7 for each) was subsequently infused for the following 300-min clamp period. In study 1, GH infusion in the basal state did not significantly alter plasma FFA or insulin levels. In contrast, GH infusion decreased insulin-stimulated glucose uptake, glycolysis, and glycogen synthesis by 32, 27, and 40%, respectively ($P < 0.05$). In study 2, GH infusion during hyperinsulinemic euglycemic clamps did not alter plasma FFA or insulin levels ($P > 0.05$). GH infusion had no effect on insulin-stimulated glucose uptake during the initial 150 min but eventually decreased insulin-stimulated glucose uptake by 37% ($P < 0.05$), similar to the

results in study 1. These data indicate that GH induces peripheral insulin resistance independent of plasma FFA and insulin levels. The induction of insulin resistance was preceded by suppression of glycogen synthesis, consistent with the hypothesis that metabolic impairment precedes and causes development of peripheral insulin resistance.

CONTROLLED TERM: Check Tags: Male
Animals
***Fatty Acids, Nonesterified: BL, blood**
Glucose: ME, metabolism
Glucose Clamp Technique
Glycogen: BI, biosynthesis
Glycolysis: DE, drug effects
*Growth Hormone: PD, pharmacology
Humans
***Insulin: BL, blood**
Insulin: PD, pharmacology
***Insulin Resistance**
Rats
Rats, Wistar
Recombinant Proteins
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Time Factors

CAS REGISTRY NO.: 11061-68-0 (Insulin); 50-99-7 (Glucose); 9002-72-6 (Growth Hormone); 9005-79-2 (Glycogen)

CHEMICAL NAME: 0 (Fatty Acids, Nonesterified); 0 (Recombinant Proteins)

L125 ANSWER 10 OF 76 MEDLINE on STN

ACCESSION NUMBER: 1999191897 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 10094109

TITLE: Chronic physiologic hyperinsulinemia impairs suppression of plasma free fatty acids and increases de novo lipogenesis but does not cause dyslipidemia in conscious normal rats.

AUTHOR: Koopmans S J; Kushwaha R S; DeFronzo R A

CORPORATE SOURCE: Department of Medicine, University of Texas Health Science Center, San Antonio 78284-7886, USA.

SOURCE: Metabolism: clinical and experimental, **(1999 Mar)** Vol. 48, No. 3, pp. 330-7.
Journal code: 0375267. ISSN: 0026-0495.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199904

ENTRY DATE: Entered STN: 26 Apr 1999
Last Updated on STN: 26 Apr 1999
Entered Medline: 13 Apr 1999

ABSTRACT:
Type 2 diabetes mellitus and obesity are characterized by fasting hyperinsulinemia, insulin resistance with respect to glucose metabolism, elevated plasma free fatty acid (FFA) levels, hypertriglyceridemia, and decreased high-density lipoprotein (HDL) cholesterol. An association between hyperinsulinemia and dyslipidemia has been suggested, but the causality of the relationship remains uncertain. Therefore, we infused eight 12-week-old male catheterized conscious normal rats with insulin (1 mU/min) for 7 days while maintaining euglycemia using a modification of the glucose clamp technique. Control rats (n = 8) received vehicle infusion. Baseline FFAs were 1.07+/-0.13 mmol/L, decreased to 0.57+/-0.10 (P < .05) upon initiation of the insulin infusion, and gradually increased to 0.95+/-0.12 by day 7 (P = NS vbaseline). On day 7 after a 6-hour fast, plasma insulin, glucose, and FFA levels in

control and chronically hyperinsulinemic rats were 32+/-5 versus 116+/-21 mU/L (P < .005), 122+/-4 versus 129+/-8 mg/dL (P = NS), and 1.13+/-0.18 versus 0.95+/-0.12 mmol/L (P = NS); total plasma triglyceride and cholesterol levels were 78+/-7 versus 66+/-9 mg/dL (P = NS) and 50+/-3 versus 47+/-2 mg/dL (P = NS), respectively. Very-low-density lipoprotein (VLDL) + intermediate-density lipoprotein (IDL), low-density lipoprotein (LDL), and HDL2 and HDL3 subfractions of plasma triglyceride and cholesterol were similar in control and hyperinsulinemic rats. Plasma FFA correlated positively with total (r = .61, P < .005) triglycerides. On day 7 after an 8-hour fast, hyperinsulinemic-euglycemic clamps with 3-3H-glucose infusion were performed in all rats. Chronically hyperinsulinemic rats showed peripheral insulin resistance (glucose uptake, 15.8+/-0.8 v 19.3+/-1.4 mg/kg x min, P < .02) but normal suppression of hepatic glucose production (HGP) compared with control rats (4.3+/-1.0 v 5.6+/-1.4 mg/kg x min, P = NS). De novo tissue lipogenesis (3-3H-glucose incorporation into lipids) was increased in chronically hyperinsulinemic versus control rats (0.90+/-0.10 v 0.44+/-0.08 mg/kg x min, P < .005). In conclusion, chronic physiologic hyperinsulinemia (1) causes insulin resistance with regard to the suppression of plasma FFA levels and increases lipogenesis; (2) induces peripheral but not hepatic insulin resistance with respect to glucose metabolism; and (3) does not cause an elevation in VLDL-triglyceride or a reduction in HDL-cholesterol.

CONTROLLED TERM: Check Tags: Male
Animals
Blood Glucose: ME, metabolism
Chronic Disease
Energy Metabolism: PH, physiology
***Fatty Acids, Nonesterified: BL, blood**
Glucose Clamp Technique
Glycogen: BI, biosynthesis
Glycolysis: DE, drug effects
***Hyperinsulinism: BL, blood**
Hyperinsulinism: CO, complications
***Hyperlipidemia: BL, blood**
Hyperlipidemia: ET, etiology
Hypoglycemic Agents: PD, pharmacology
Insulin: BL, blood
Insulin: PD, pharmacology
Insulin Resistance
*Lipids: BI, biosynthesis
Lipoproteins: BL, blood
Liver: ME, metabolism
Rats
Rats, Sprague-Dawley
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, Non-P.H.S.
Triglycerides: BL, blood

CAS REGISTRY NO.: 11061-68-0 (Insulin); 9005-79-2 (Glycogen)

CHEMICAL NAME: 0 (Blood Glucose); 0 (Fatty Acids, Nonesterified); 0 (Hypoglycemic Agents); 0 (Lipids); 0 (Lipoproteins); 0 (Triglycerides)

L125 ANSWER 11 OF 76 MEDLINE on STN

ACCESSION NUMBER: 97474759 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 9329954

TITLE: Myocardial insulin resistance in patients with syndrome X.

AUTHOR: Botker H E; Moller N; Schmitz O; Bagger J P; Nielsen T T

CORPORATE SOURCE: Department of Cardiology, Skejby Hospital, University Hospital Aarhus, DK-8200 Aarhus N, Denmark.

SOURCE: The Journal of clinical investigation, **(1997 Oct 15)** Vol. 100, No. 8, pp. 1919-27.

Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 24 Dec 1997
Last Updated on STN: 24 Dec 1997
Entered Medline: 20 Nov 1997

ABSTRACT:
Insulin resistance is common in patients with angina pectoris, a positive exercise electrocardiogram, and normal coronary angiograms (syndrome X). It is still not known whether insulin resistance affects the cardiac muscle itself and, if so, whether insulin resistance involves myocardial hemodynamics and energy metabolism. We investigated hemodynamics as well as metabolite exchanges across the heart and the forearm in eight patients with syndrome X and eight control subjects during a baseline period after an overnight fast and during a hyperinsulinemic-euglycemic clamp. Myocardial hemodynamics and metabolism were studied at rest, during pace stress, and in the recovery period after pacing. Neither coronary sinus blood flow nor forearm blood flow differed between the groups before and during the clamp. Whole body insulin-stimulated glucose uptake was decreased in the patients (15.6+/-2.1 vs. 23.1+/-2.0 micromol x kg-1 x min-1). Insulin-stimulated glucose uptake in the forearm and the cardiac muscle was equally reduced in the patients (46+/-5 and 48+/-5%). Myocardial glucose uptake correlated with total arterial delivery in the control subjects ($r = 0.63$, $P < 0.01$), but not in patients ($r = 0.22$, $P = 0.13$). Carbohydrate and lipid oxidation was similar in the two groups at rest, and changes during the clamp were not different in control subjects and patients either at rest, during pacing, or in the recovery period. Patients with syndrome X exhibit myocardial insulin resistance, but cardiac energy metabolism remains unaffected. In patients with syndrome X, insulin-stimulated glucose uptake is independent from myocardial blood flow.

CONTROLLED TERM: Check Tags: Female; Male
Blood Glucose: ME, metabolism
Energy Metabolism
Fatty Acids, Nonesterified: BL, blood
Fluorine Radioisotopes
Fluorodeoxyglucose F18: DU, diagnostic use
Glucose Clamp Technique
Glycolysis
*Heart: DE, drug effects
Heart Catheterization
Hemodynamic Processes
Humans
***Insulin Resistance**
*Microvascular Angina: DI, diagnosis
Middle Aged
Muscle, Skeletal: ME, metabolism
Potassium: BL, blood
Research Support, Non-U.S. Gov't
Tomography, Emission-Computed
CAS REGISTRY NO.: 63503-12-8 (Fluorodeoxyglucose F18); 7440-09-7 (Potassium)
CHEMICAL NAME: 0 (Blood Glucose); 0 (Fatty Acids, Nonesterified); 0 (Fluorine Radioisotopes)

L125 ANSWER 12 OF 76 MEDLINE on STN
ACCESSION NUMBER: 97308004 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9165230
TITLE: Reversibility of insulin resistance in obese diabetic patients: role of plasma lipids.

AUTHOR: Mingrone G; DeGaetano A; Greco A V; Capristo E; Benedetti G; Castagneto M; Gasbarrini G
CORPORATE SOURCE: Istituto di Medicina Interna e Geriatria, Universita Cattolica S. Cuore, Rome, Italy.
SOURCE: Diabetologia, **(1997 May)** Vol. 40, No. 5, pp. 599-605.
Journal code: 0006777. ISSN: 0012-186X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 5 Aug 1997
Last Updated on STN: 5 Aug 1997
Entered Medline: 18 Jul 1997

ABSTRACT:
The aim of the present study was to measure whole body **glucose** uptake (M) and oxidation rate by euglycaemic hyperinsulinaemic clamp and indirect calorimetry in 7 morbidly obese subjects (BMI > 40 kg/m2) at three time points: before bilio-pancreatic diversion (BPD) surgery (Ob); 3 months after surgery POI; and after reaching stable body weight, at least 2 years after surgery POII. A group of 7 control subjects (C), matched groupwise for sex, age and BMI with POII patients, was also studied. The M value at POI was significantly higher than at Ob (49.12 +/- 8.57 vs 18.14 +/- 8.57 mumol.kg-1.min-1). No statistical difference was observed between the POII and C groups. Similarly, ***glucose*** oxidation rate was significantly increased at POI with respect to Ob (24.2 +/- 7.23 vs 9.42 +/- 3.91 mumol.kg-1.min-1) and was not significantly different between POII and C. Basal levels of non-esterified fatty acids (NEFA) decreased significantly both from Ob to POI and from POI to POII (1517.1 +/- 223.9 vs 1039.6 +/- 283.4 vs 616.0 +/- 77.6 mumol.1(-1). The same applied to basal plasma triglycerides (2.07 +/- 0.77 vs 1.36 +/- 0.49 vs 0.80 +/- 0.19 g.1(-1). Weight decreased mainly in the late postoperative period (POI to POII 124.28 +/- 11.22 to 69.71 +/- 11.78, 83% of total decrement), rather than in the early postoperative period (Ob to POI 135.25 +/- 14.99 to 124.28 +/- 11.22 kg, 17% of total decrement). We also report the clinical case of a young woman of normal weight, who underwent BPD for chylomicronaemia (secondary to familial lipoprotein lipase deficiency), whose M value, plasma insulin and blood **glucose** levels were normalized upon normalization of serum NEFA and triglyceride levels as determined by the therapeutic lipid malabsorption. In conclusion, in obese diabetic patients lipid malabsorption induced by BPD causes a definite enhancement of insulin sensitivity and **glucose** tolerance. This improvement in metabolism is noticeable before the surgery has major effects on body weight. These observations suggest that lowered plasma lipids, rather than weight loss per se, are the cause of the reversibility of insulin resistance.

CONTROLLED TERM: Check Tags: Female; Male
Adult
Biliopancreatic Diversion
Body Composition
Diabetes Mellitus: BL, blood
*Diabetes Mellitus: PP, physiopathology
*Energy Metabolism
Fatty Acids, Nonesterified: BL, blood
Follow-Up Studies
Glucose: ME, metabolism
Glucose Clamp Technique
Glycolysis
Humans
Infusions, Intravenous
Insulin: AD, administration & dosage

Insulin: BL, blood
Insulin: PD, pharmacology
***Insulin Resistance**
***Obesity**
Obesity, Morbid: BL, blood
***Obesity, Morbid: PP, physiopathology**
Obesity, Morbid: SU, surgery
Reference Values
Time Factors
Triglycerides: BL, blood
Weight Loss
CAS REGISTRY NO.: 11061-68-0 (Insulin); **50-99-7 (Glucose)**
CHEMICAL NAME: 0 (Fatty Acids, Nonesterified); 0 (Triglycerides)

L125 ANSWER 13 OF 76 MEDLINE on STN
ACCESSION NUMBER: 97101444 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8945970
TITLE: Changes in insulin action, triglycerides, and lipid composition during sucrose feeding in rats.
AUTHOR: Pagliassotti M J; Prach P A; Koppenhafer T A; Pan D A
CORPORATE SOURCE: Section of Pediatric Nutrition, University of Colorado Health Sciences Center, Denver 80262, USA.
CONTRACT NUMBER: DK-47416 (NIDDK)
SOURCE: The American journal of physiology, **(1996 Nov)** Vol. 271, No. 5 Pt 2, pp. R1319-26.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 28 Jan 1997
Last Updated on STN: 28 Jan 1997
Entered Medline: 3 Jan 1997

ABSTRACT:
In the present study, the time course of change in sucrose-induced insulin resistance, triglyceride (TG) concentration, and liver fatty acid composition was examined. Male rats (n = 8-10/group per time point) was fed a high-starch (ST) diet for 2 wk and were then equicalorically fed ST or a high-sucrose (SU) diet for 1, 2, 5, or 8 wk. Body weight and percent body fat were similar between ST and SU diets at all time points. Glucose infusion rate (GIR) was significantly ($P < 0.05$) lower in the SU diet (9.2 +/- 0.9, 7.4 +/- 0.5, 6.2 +/- 1.0, and 6.0 +/- 0.9 mg.kg-1.min-1) vs. the ST diet (15.1 +/- 1.7, 15.7 +/- 0.7, 14.7 +/- 1.9, and 14.2 +/- 0.9 mg.kg-1.min-1) at 1, 2, 5, and 8 wk, respectively. Reduced suppression of glucose appearance accounted for 85, 50, 45, and 40% of the reduction in GIR at these same time points. Muscle glycogen synthesis was reduced ($P < 0.05$ vs. ST diet) in the SU diet at 2, 5, and 8 wk. Fasting plasma TG concentration was inversely related ($r = -0.79$, $P < 0.001$) to muscle glycogen synthesis, and liver TG concentration was positively related ($r = 0.59$, $P < 0.01$) to glucose appearance. Liver fatty acid composition was similar between diet groups. In summary, the SU diet produced insulin resistance in liver before muscle. TG concentration appears to be related to sucrose-induced insulin resistance in liver and muscle.
CONTROLLED TERM: Check Tags: Male
Animals
Blood Glucose: AN, analysis
*Dietary Sucrose: PD, pharmacology
***Fatty Acids: ME, metabolism**
Glucose: PK, pharmacokinetics
Glucose: PD, pharmacology

Glycogen: BI, biosynthesis
Glycolysis
Insulin: BL, blood
***Insulin Resistance**
*Liver: ME, metabolism
Muscles: ME, metabolism
Rats
Rats, Wistar
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
***Triglycerides: BL, blood**
Triglycerides: ME, metabolism

CAS REGISTRY NO.: 11061-68-0 (Insulin); 50-99-7 (Glucose); 9005-79-2 (Glycogen)
CHEMICAL NAME: 0 (Blood Glucose); 0 (Dietary Sucrose); 0 (Fatty Acids); 0 (Triglycerides)

L125 ANSWER 14 OF 76 MEDLINE on STN
ACCESSION NUMBER: 97088508 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8934446
TITLE: Chronic free fatty acid infusion in rats results in insulin resistance but no alteration in insulin-responsive glucose transporter levels in skeletal muscle.
AUTHOR: Magnan C; Gilbert M; Kahn B B
CORPORATE SOURCE: Laboratoire de Physiopathologie de la Nutrition, CNRS U 307, Universite Paris 7, France.
CONTRACT NUMBER: DK R01-43051 (NIDDK)
SOURCE: Lipids, **(1996 Nov)** Vol. 31, No. 11, pp. 1141-9.
Journal code: 0060450. ISSN: 0024-4201.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 14 Apr 1997
Last Updated on STN: 14 Apr 1997
Entered Medline: 28 Mar 1997

ABSTRACT:
To investigate the mechanism by which free fatty acids (FFA) affect glucose uptake, we studied the effect of chronic elevation (24 h) of plasma FFA in rats on whole body glucose disposal and glucose utilization index (GUI) in the basal state and under a euglycemic hyperinsulinemic clamp in relation to the amount of insulin-responsive glucose transporter (IRGT, i.e., GLUTU) protein in different muscles (oxidative and glycolytic) and adipose tissue. Infusion of intralipid in the basal state led to a approximately 40% increase in whole body glucose uptake and a approximately 250% increase in GUI in adipose tissue as compared to control rats. There was no change in the amount of IRGT protein in any of the muscle types whereas in fat depots it was either unchanged or decreased. Under moderate of supraphysiological hyperinsulinemia, increment of whole body glucose disposal was significantly lower in intralipid perfused rats when compared to controls (approximately 110 microU/mL: 0.7 +/- 0.1 vs. 1.3 +/- 0.1 mg/min, $P < 0.02$; approximately 1000 microU/mL: 3.0 +/- 0.2 vs. 3.9 +/- 0.4 mg/min, $P < 0.02$). Under moderate hyperinsulinemia stimulation, GUI was significantly reduced in different muscles and adipose tissue as compared to controls. We conclude that peripheral insulin resistance which occurs after elevation of plasma FFA levels does not seem to be explained by changes in the amount of IRGT protein in either oxidative or glycolytic skeletal muscle. Thus fatty acid infusion appears to be associated with a defect in IRGT translocation to the plasma membrane, fusion with the membrane, or intrinsic activity.

CONTROLLED TERM: Check Tags: Female
Adipose Tissue: DE, drug effects
Adipose Tissue: ME, metabolism
Animals
Biological Transport, Active
Blood Glucose: ME, metabolism
Fat Emulsions, Intravenous: AD, administration & dosage
***Fatty Acids, Nonesterified: AD, administration & dosage**
Fatty Acids, Nonesterified: BL, blood
Glucose: ME, metabolism
Glucose Transporter Type 4
Glycogen: ME, metabolism
Glycolysis
Hyperlipidemia: ME, metabolism
Infusions, Intravenous
Insulin: BL, blood
Insulin Resistance: PH, physiology
Kinetics
Liver Glycogen: ME, metabolism
*Monosaccharide Transport Proteins: ME, metabolism
*Muscle Proteins
*Muscle, Skeletal: DE, drug effects
*Muscle, Skeletal: ME, metabolism
Rats
Rats, Wistar
Research Support, U.S. Gov't, P.H.S.

CAS REGISTRY NO.: 11061-68-0 (Insulin); 50-99-7 (Glucose); 9005-79-2 (Glycogen)

CHEMICAL NAME: 0 (Blood Glucose); 0 (Fat Emulsions, Intravenous); 0 (Fatty Acids, Nonesterified); 0 (Glucose Transporter Type 4); 0 (Liver Glycogen); 0 (Monosaccharide Transport Proteins); 0 (Muscle Proteins); 0 (Slc2a4 protein, rat)

L125 ANSWER 15 OF 76 MEDLINE on STN

ACCESSION NUMBER: 96198508 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 8621018

TITLE: Metabolic impairment precedes insulin resistance in skeletal muscle during high-fat feeding in rats.

AUTHOR: Kim J K; Wi J K; Youn J H

CORPORATE SOURCE: Department of Physiology and Biophysics, University of Southern California, School of Medicine, Los Angeles 90033, USA.

CONTRACT NUMBER: NIA T32-AG00093 (NIA)
R-29 DK-47947 (NIDDK)

SOURCE: Diabetes, **(1996 May)** Vol. 45, No. 5, pp. 651-8.
Journal code: 0372763. ISSN: 0012-1797.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199606

ENTRY DATE: Entered STN: 27 Jun 1996
Last Updated on STN: 3 Feb 1997
Entered Medline: 14 Jun 1996

ABSTRACT:
To examine whether impairment of intracellular glucose metabolism precedes insulin resistance, we determined the time courses of changes in insulin-stimulated glucose uptake, glycolysis, and glycogen synthesis during high-fat feeding in rats. Animals were fed with a high-fat (66.5%) diet ad

libitum for 0, 2, 4, 7, or 14 days (n = 10-11 in each group) after 5 days of a low-fat (12.5%) diet. Submaximal and maximal insulin-stimulated glucose fluxes were estimated in whole body and individual skeletal muscles using the glucose clamp technique combined with D-[3-3H]glucose infusion and 2-[1-14C]deoxyglucose injection. Both submaximal and maximal insulin-stimulated glucose uptake in whole body decreased gradually with high-fat feeding. However, the decreases were minimal and not statistically significant during the initial few days (i.e., 2 and 4 days) of high-fat feeding ($P > 0.05$). In contrast, insulin-stimulated whole-body glycolysis (both maximal and submaximal) significantly decreased by approximately 30% with 2 days of high-fat feeding and remained suppressed thereafter ($P < 0.05$). Similar patterns of changes in insulin-stimulated glucose uptake and glycolysis were also observed in skeletal muscle. Insulin-stimulated glycogen synthesis and glucose-6-phosphate (G-6-P) concentrations in skeletal muscle increased significantly during the initial few days of high-fat feeding and gradually returned to control levels by day 14, suggesting that increased G-6-P concentrations were responsible for increased glycogen synthesis. Thus, suppression of insulin-stimulated glycolysis and a compensatory increase in glycogen synthesis (presumably arising from the glucose-fatty acid cycle) preceded decreases in insulin-stimulated glucose uptake in skeletal muscle during high-fat feeding. These findings suggest that the insulin resistance may develop as a secondary response to impaired intracellular glucose metabolism.

CONTROLLED TERM: Check Tags: Male
Animals
Blood Glucose: ME, metabolism
Comparative Study
Deoxyglucose: ME, metabolism
*Diet, Fat-Restricted
*Dietary Fats
Fatty Acids, Nonesterified: BL, blood
*Glucose: ME, metabolism
Glucose Clamp Technique
Glycogen: BI, biosynthesis
Glycolysis: DE, drug effects
Insulin: AD, administration & dosage
Insulin: PD, pharmacology
***Insulin Resistance**
Kinetics
Muscle, Skeletal: DE, drug effects
Muscle, Skeletal: ME, metabolism
*Muscle, Skeletal: PH, physiology
Rats
Rats, Wistar
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Time Factors
Tritium

CAS REGISTRY NO.: 10028-17-8 (Tritium); 11061-68-0 (Insulin); 154-17-6 (Deoxyglucose); 50-99-7 (Glucose); 9005-79-2 (Glycogen)

CHEMICAL NAME: 0 (Blood Glucose); 0 (Dietary Fats); 0 (Fatty Acids, Nonesterified)

L125 ANSWER 16 OF 76 MEDLINE on STN

ACCESSION NUMBER: 95355555 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 7629243

TITLE: Contribution of obesity to insulin resistance in noninsulin-dependent diabetes mellitus.

AUTHOR: Perriello G; Misericordia P; Volpi E; Pampanelli S; Santeusanio F; Brunetti P; Bolli G B

CORPORATE SOURCE: Dipartimento di Medicina Interna e Scienze Endocrine e Metaboliche, University of Perugia.
SOURCE: The Journal of clinical endocrinology and metabolism, (1995 Aug) Vol. 80, No. 8, pp. 2464-9.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 21 Sep 1995
Last Updated on STN: 21 Sep 1995
Entered Medline: 7 Sep 1995

ABSTRACT:
Inasmuch as previous studies have obtained conflicting results on the contribution of obesity to insulin resistance in noninsulin-dependent diabetes mellitus (NIDDM), we studied 10 nonobese and 10 obese NIDDM patients with the isoglycemic-(approximately 10 mmol/L)-hyperinsulinemic clamp (two insulin infusions of 4 and 40 mU/m-2 min-1), combined with [3-3H]**glucose** infusion and indirect calorimetry. As compared with nonobese patients, obese NIDDM patients had higher baseline peripheral and estimated portal plasma insulin concentrations (113 +/- 18 vs. 46 +/- 3 pmol/L and 288 +/- 53 vs. 98 +/- 6 pmol/L, respectively; P < 0.05) and less suppressed endogenous insulin production during clamp. Hepatic **glucose** production was greater in obese than in nonobese patients (basal, 16 +/- 1.1 vs. 12 +/- 0.5 mumol/kg-1 fat-free mass (FFM) min-1; clamp, 5.7 +/- 0.5 vs. 2.8 +/- 0.2 mumol/kg-1 FFM min-1, P < 0.05). **Glucose** utilization increased to a lesser extent in obese than in nonobese patients (49 +/- 5 vs. 73 +/- 7 mumol/kg-1 FFM min-1, P < 0.05) during clamp because of a lower increase in nonoxidative ***glucose*** metabolism (30 +/- 5 vs. 50 +/- 7 mumol/kg-1 FFM min-1, P < 0.05). Plasma free fatty acid concentrations and rates of lipid oxidation were greater in obese (P < 0.05) patients and correlated with hepatic ***glucose*** production (r = 0.79 and 0.50, P < 0.05). In conclusion, obesity exaggerates hepatic as well as extra-hepatic insulin resistance in NIDDM. The impaired inhibition of pancreatic beta-cell function by exogenous insulin contributes to exaggerated hyperinsulinemia in obese NIDDM.

CONTROLLED TERM: Check Tags: Female; Male
***Blood Glucose: ME, metabolism**
C-Peptide: BL, blood
Comparative Study
Diabetes Mellitus: BL, blood
*Diabetes Mellitus: ME, metabolism
Diabetes Mellitus, Type 2: BL, blood
*Diabetes Mellitus, Type 2: ME, metabolism
*Energy Metabolism
Fatty Acids, Nonesterified: BL, blood
Glucose Clamp Technique
Glycolysis
Humans
Infusions, Intravenous
Insulin: AD, administration & dosage
***Insulin: BL, blood**
Insulin: PD, pharmacology
***Insulin Resistance**
Liver: ME, metabolism
Middle Aged
***Obesity**
Portal System
Regression Analysis
Research Support, Non-U.S. Gov't

CAS REGISTRY NO.: 11061-68-0 (Insulin)
CHEMICAL NAME: 0 (Blood **Glucose**); 0 (C-Peptide); 0 (Fatty Acids, Nonesterified)

L125 ANSWER 17 OF 76 MEDLINE on STN
ACCESSION NUMBER: 95272400 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7752903
TITLE: (-)-BM 13.0913: a new oral antidiabetic agent that improves insulin sensitivity in animal models of type II (non-insulin-dependent) diabetes mellitus.
AUTHOR: Freund P; Wolff H P; Kuhnle H F
CORPORATE SOURCE: Department of Medical Research/Diabetes, Boehringer, Mannheim, Germany.
SOURCE: Metabolism: clinical and experimental, **(1995 May)** Vol. 44, No. 5, pp. 570-6.
Journal code: 0375267. ISSN: 0026-0495.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 29 Jun 1995
Last Updated on STN: 6 Feb 1998
Entered Medline: 21 Jun 1995

ABSTRACT:
Insulin resistance is one of the key features of non-insulin-dependent diabetes mellitus (NIDDM). Therefore, a drug that causes an improvement in insulin sensitivity would be of great interest for the treatment of NIDDM. In addition to the insulin-sensitizing thiazolidinediones, we have found another class of insulin-sensitizing agents: the alpha-activated carbonic acids. (-)-BM 13.0913, a member of this class, was effective in improving insulin resistance in hyperinsulinemic and hypoinsulinemic insulin-resistant animal models of NIDDM. The 50% effective dose (ED50) for the glucose-lowering action was 4, 2.4, and 8 mg/kg in ob/ob, yellow KK, and db/db mice, respectively. The ED50 for the insulin-lowering action was 14.5, 5, and 26 mg/kg. This rightward shift of the dose-response curve for insulin indicates that improving glucose homeostasis is the primary effect of the drug, followed by an insulin-decreasing action. This effect on glucose homeostasis may be brought about by sensitizing peripheral target tissues to the effects of insulin. An increase in deoxyglucose uptake and glucose oxidation measured in adipocytes from rats that had been treated for 14 days with (-)-BM 13.0913 supports this conclusion. Glucose uptake and oxidation was increased at all insulin concentrations tested, suggesting an improved responsiveness. Insulin sensitivity in adipocytes was not influenced by the drug. Studies in the moderately hypoinsulinemic, low-dose streptozotocin (STZ) diabetic rat with a residual insulin concentration showed a decrease in blood glucose concentrations, as well as a decrease in urinary glucose. (ABSTRACT TRUNCATED AT 250 WORDS)

CONTROLLED TERM: Check Tags: Female; Male
Adipocytes: DE, drug effects
Adipocytes: ME, metabolism
Administration, Oral
Animals
Blood Glucose: DE, drug effects
*Blood Glucose: ME, metabolism
Comparative Study
Diabetes Mellitus, Experimental: BL, blood
*Diabetes Mellitus, Experimental: DT, drug therapy
Diabetes Mellitus, Experimental: PP, physiopathology
Diabetes Mellitus, Type 2: BL, blood
*Diabetes Mellitus, Type 2: DT, drug therapy

Diabetes Mellitus, Type 2: PP, physiopathology
Glycolysis: DE, drug effects
***Heptanoic Acids: PD, pharmacology**
*Hypoglycemic Agents: PD, pharmacology
In Vitro
***Insulin: BL, blood**
*Insulin: PD, pharmacology
Insulin: SE, secretion
***Insulin Resistance**
Kinetics
Lipids: BL, blood
Mice
Mice, Inbred C57BL
Mice, Inbred Strains
Mice, Obese
Rats
Rats, Inbred Lew
Time Factors

CAS REGISTRY NO.: 11061-68-0 (Insulin); 145096-04-4 (2-(4-methylphenoxy)-7-(4-chlorophenyl)heptanoic acid)
CHEMICAL NAME: 0 (Blood Glucose); 0 (Heptanoic Acids); 0 (Hypoglycemic Agents); 0 (Lipids)

L125 ANSWER 18 OF 76 MEDLINE on STN
ACCESSION NUMBER: 95278656 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7758874
TITLE: Excessive glucose production, rather than insulin resistance, accounts for hyperglycaemia in recent-onset streptozotocin-diabetic rats.
AUTHOR: Burcelin R; Eddouks M; Maury J; Kande J; Assan R; Girard J
CORPORATE SOURCE: Service de Diabetologie Hopital Bichat, Paris, France.
SOURCE: Diabetologia, **(1995 Mar)** Vol. 38, No. 3, pp. 283-90.
Journal code: 0006777. ISSN: 0012-186X.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 7 Jul 1995
Last Updated on STN: 7 Jul 1995
Entered Medline: 26 Jun 1995

ABSTRACT:
Glucose production and utilization and activities of key enzymes involved in liver and muscle glucose metabolism were studied in post-absorptive streptozotocin-diabetic rats after 12 h of severe hyperglycaemia (17.5 +/- 0.5 mmol/l) and insulinopenia (5 +/- 1 microU/ml). Basal glucose production was increased: 36.6 +/- 3.0 mg.kg.min-1, vs 24.4 +/- 2.5 in controls ($p < 0.05$); liver glycogen concentration was decreased by 40% ($p < 0.05$); liver phosphoenolpyruvate carboxykinase and glucose-6-phosphatase activities were increased by 375 and 156%, respectively ($p < 0.001$ and < 0.01). During a euglycaemic clamp at a plasma insulin level of 200 microU/ml, glucose production was totally suppressed in controls, but persisted at 20% of basal in diabetic rats. In these rats, glucose production was suppressed at a plasma insulin level of 2500 microU/ml. Basal whole body glucose utilization rate, 2-deoxy-1-[3H]-D-glucose ([3H]-2DG) uptake by muscles and muscle glycogen concentrations were similar in both groups, as well as total and active forms of pyruvate dehydrogenase and glycogen synthase activities. During the euglycaemic clamp, the total body glucose utilization rates and [3H]-2DG uptake by muscles were similar in control and diabetic rats at a plasma insulin level

of 200 microU/ml, but lower in diabetic rats at a plasma insulin level of 2500 microU/ml. We conclude 1) in recent-onset severely insulinopenic rats, an excessive glucose production via gluconeogenesis prevailed, mainly accounting for the concomitant hyperglycaemia. This excess glucose output cannot be attributed to liver insulin resistance: the gluconeogenic pathway is physiologically less sensitive than glycogenolysis to the inhibition by insulin.(ABSTRACT TRUNCATED AT 250 WORDS)

CONTROLLED TERM: Check Tags: Male
Adipose Tissue: ME, metabolism
Animals
Blood Glucose: ME, metabolism
Brown Fat: ME, metabolism
Comparative Study
Deoxyglucose: ME, metabolism
*Diabetes Mellitus, Experimental: ME, metabolism
Diabetes Mellitus, Experimental: PP, physiopathology
Fatty Acids, Nonesterified: BL, blood
Glucagon: BL, blood
*Glucose: ME, metabolism
Glucose Clamp Technique
Glycogen: ME, metabolism
Glycolysis
Hyperglycemia: ET, etiology
Hyperglycemia: ME, metabolism
*Hyperglycemia: PP, physiopathology
Insulin: BL, blood
***Insulin Resistance**
*Liver: ME, metabolism
Liver Glycogen: ME, metabolism
Muscle, Skeletal: ME, metabolism
Myocardium: ME, metabolism
Organ Specificity
Rats
Rats, Wistar
Reference Values
Research Support, Non-U.S. Gov't

CAS REGISTRY NO.: 11061-68-0 (Insulin); 154-17-6 (Deoxyglucose); 50-99-7 (Glucose); 9005-79-2 (Glycogen); 9007-92-5 (Glucagon)

CHEMICAL NAME: 0 (Blood Glucose); 0 (Fatty Acids, Nonesterified); 0 (Liver Glycogen)

L125 ANSWER 19 OF 76 MEDLINE on STN

ACCESSION NUMBER: 92267256 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 1587397

TITLE: Intracellular defects in **glucose** metabolism in obese patients with NIDDM.

AUTHOR: Kelley D E; Mokan M; Mandarino L J

CORPORATE SOURCE: Department of Medicine, Eye and Ear Institute of Pittsburgh, PA 15213.

CONTRACT NUMBER: M01-RR-00056 (NCRR)
R01-DK-41075 (NIDDK)

SOURCE: Diabetes, **(1992 Jun)** Vol. 41, No. 6, pp. 698-706.
Journal code: 0372763. ISSN: 0012-1797.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199206

ENTRY DATE: Entered STN: 10 Jul 1992
Last Updated on STN: 3 Feb 1997

Entered Medline: 19 Jun 1992

ABSTRACT:
Skeletal muscle insulin resistance in obese patients with non-insulin-dependent diabetes mellitus (NIDDM) is characterized by decreased **glucose** uptake. Although reduced glycogen synthesis is thought to be the predominant cause for this deficit, studies supporting this notion often have been conducted at supraphysiological insulin concentrations in which **glucose** storage is the overwhelming pathway of **glucose** disposal. However, at lower, more physiological insulin concentrations, decreased muscle ***glucose*** oxidation could play a significant role. This study was undertaken to determine whether, under euglycemic conditions, insulin resistance for leg muscle **glucose** uptake in NIDDM patients is due primarily to decreased **glucose** storage or to oxidation. The leg balance technique and leg indirect calorimetry were used under steady-state euglycemic conditions to estimate muscle **glucose** uptake, storage, and oxidation in eight moderately obese NIDDM patients and eight matched-control subjects. Leg muscle biopsies also were performed to determine whether alterations in muscle pyruvate dehydrogenase or glycogen synthase activities could explain defects in **glucose** oxidation or storage. At insulin concentrations of approximately 500-600 pM, leg **glucose** uptake, oxidation, and storage in the NIDDM group (2.03 +/- 0.42, 1.00 +/- 0.13, 0.66 +/- 0.36 mumol.min-1.100 ml-1) were significantly lower (P less than 0.05) than rates in control subjects (5.14 +/- 0.64, 1.92 +/- 0.17, 2.80 +/- 0.54). Pyruvate dehydrogenase and glycogen synthase activities were also decreased, consistent with the in vivo metabolic defects. The average deficit in leg ***glucose*** uptake in NIDDM was 3.11 +/- 0.42 mumol.min-1.100 ml-1. (ABSTRACT TRUNCATED AT 250 WORDS)

CONTROLLED TERM: Check Tags: Male
Analysis of Variance
Blood Glucose: ME, metabolism
Carbon Dioxide: BL, blood
Diabetes Mellitus: BL, blood
*Diabetes Mellitus: ME, metabolism
Diabetes Mellitus, Type 2: BL, blood
*Diabetes Mellitus, Type 2: ME, metabolism
Fatty Acids, Nonesterified: BL, blood
***Glucose: ME, metabolism**
Glycogen Synthase: ME, metabolism
***Glycolysis**
Humans
Insulin: PD, pharmacology
Insulin Resistance
Kinetics
Middle Aged
Muscles: DE, drug effects
*Muscles: ME, metabolism
***Obesity**
Oxygen: BL, blood
Oxygen Consumption
Partial Pressure
Pyruvate Dehydrogenase Complex: ME, metabolism
Reference Values
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.

CAS REGISTRY NO.: 11061-68-0 (Insulin); 124-38-9 (Carbon Dioxide); **50-99-7 (Glucose)**; 7782-44-7 (Oxygen)

CHEMICAL NAME: 0 (Blood **Glucose**); 0 (Fatty Acids, Nonesterified); 0 (Pyruvate Dehydrogenase Complex); EC 2.4.1.11 (Glycogen Synthase)

L125 ANSWER 20 OF 76 MEDLINE on STN
ACCESSION NUMBER: 92174730 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1794264
TITLE: Insulin resistance, insulin deficiency, and non-insulin-dependent diabetes mellitus.
AUTHOR: Cerasi E
CORPORATE SOURCE: Department of Endocrinology and Metabolism, Hebrew University Hadassah Medical Center, Jerusalem, Israel..
SOURCE: Diabetes research and clinical practice, **(1991)** Vol. 14 Suppl 2, pp. S37-45.
Journal code: 8508335. ISSN: 0168-8227.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 24 Apr 1992
Last Updated on STN: 24 Apr 1992
Entered Medline: 6 Apr 1992

ABSTRACT:
Recent information suggests that type 2 diabetes mellitus (NIDDM) is associated with severe insulin resistance, but other information suggests that there is a hypoinsulinemic state. To investigate the nature of the insulin resistance, 10 newly diagnosed, mildly obese type 2 diabetics and 11 long-standing type 2 diabetics with secondary failure to sulfonylureas were studied. Insulin was given by continuous subcutaneous infusion (CSII) for two weeks. CSII produced near-normoglycemia after 1-4 days in all patients with modest amounts of insulin (0.5-0.9 U/kg/24 h). These results demonstrate that whatever insulin resistance prevails in NIDDM, it does not prevent induction of normoglycemia by insulin. This suggests that either the insulin resistance is a secondary event caused by hyperglycaemia, or that NIDDM patients are hypoinsulinemic. In further studies in vitro, the effect of **glucose** on the rate of glycolytic **glucose** utilization by isolated rat soleus muscle and on hexose transport in rat skeletal myocyte line L8 were assessed. In the first case, an increase in **glucose** concentration led to a decrease in muscle glycolysis, and in the second case a hyperglycemic concentration of ***glucose*** led to a marked reduction in hexose transport, which was fully reversible within two hours. The clinical and in vitro results plus literature data suggest that insulin resistance can be overcome by insulin in NIDDM, and that beta-cell responsiveness to **glucose** is greatly reduced in NIDDM, but the defect is restricted to the acute stimulatory phase of **glucose** induction of insulin release. If this defect can be corrected, acute insulin release will occur so that NIDDM would be cured notwithstanding the existence of insulin resistance.

CONTROLLED TERM: Check Tags: Male
Animals
Blood Glucose: ME, metabolism
Diabetes Mellitus: BL, blood
Diabetes Mellitus: DT, drug therapy
*Diabetes Mellitus: PP, physiopathology
Diabetes Mellitus, Type 2: BL, blood
Diabetes Mellitus, Type 2: DT, drug therapy
*Diabetes Mellitus, Type 2: PP, physiopathology
Glycolysis: DE, drug effects
Humans
Insulin: BL, blood
Insulin: PD, pharmacology
*Insulin: SE, secretion
*Insulin: TU, therapeutic use
Insulin Infusion Systems

***Insulin Resistance**
Muscles: DE, drug effects
*Muscles: ME, metabolism
***Obesity**
Rats
Rats, Inbred Strains
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, Non-P.H.S.
CAS REGISTRY NO.: 11061-68-0 (Insulin)
CHEMICAL NAME: 0 (Blood **Glucose**)

L125 ANSWER 21 OF 76 MEDLINE on STN
ACCESSION NUMBER: 89276198 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2543549
TITLE: Pathogenesis of hyperglycemia in genetically obese-hyperglycemic rats, Wistar fatty: presence of hepatic insulin resistance.
AUTHOR: Sugiyama Y; Shimura Y; Ikeda H
CORPORATE SOURCE: Central Research Division, Takeda Chemical Industries, Ltd., Osaka, Japan.
SOURCE: Endocrinologia japonica, **(1989 Feb)** Vol. 36, No. 1, pp. 65-73.
Journal code: 0376546. ISSN: 0013-7219.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198907
ENTRY DATE: Entered STN: 9 Mar 1990
Last Updated on STN: 9 Mar 1990
Entered Medline: 14 Jul 1989

ABSTRACT:
The present studies were designed to clarify the contribution of the liver to the development of hyperglycemia in Wistar fatty rats. The hepatic activities of insulin-inducible enzymes involved in glycolysis (glucokinase; GK and pyruvate kinase) and lipogenesis (**glucose**-6-phosphate dehydrogenase), were higher in fatty rats than in lean rats at 4 and 8 weeks of age because of the higher insulin levels in the former. Thereafter, the GK activities of fatty rats decreased slightly in spite of severe hyperinsulinemia, and did not differ from those of lean rats. In addition, fatty rats had higher levels of insulin-suppressible gluconeogenic enzymes, **glucose**-6-phosphatase (G6Pase) and fructose-1, 6-diphosphatase. These findings indicate that the hepatic enzymes of fatty rats are resistant to insulin. This postulation was supported by the fact that the hepatic enzyme activities of fatty rats showed a lower response to changes in plasma insulin levels produced by fasting and refeeding. The G6Pase/GK ratio, which indicates net **glucose** handling in the liver, increased in fatty rats and decreased in lean rats with advancing age, suggesting that hepatic **glucose** production in fatty rats becomes dominant with advancing age. The changes in hepatic glycolytic intermediates supported this suggestion; the glycolytic steps both from **glucose** to ***glucose*** -6-phosphate and from phospho-enolpyruvate to pyruvate in fatty rats were accelerated at 5 weeks of age, but suppressed at 12 weeks of age. These results indicate that insulin resistance in the hepatic enzyme regulation may contribute to the development of hyperglycemia in Wistar fatty rats.
CONTROLLED TERM: Check Tags: Male
Aging: ME, metabolism
Animals
Blood Glucose: ME, metabolism
Body Weight
Comparative Study

Fasting
Food
Fructose-Bisphosphatase: ME, metabolism
Glucokinase: ME, metabolism
Gluconeogenesis
Glucose-6-Phosphatase: ME, metabolism
Glucosephosphate Dehydrogenase: ME, metabolism
Glycolysis: DE, drug effects
*Hyperglycemia: ET, etiology
Hyperglycemia: ME, metabolism
Insulin: BL, blood
Insulin: PD, pharmacology
***Insulin Resistance**
Liver: DE, drug effects
*Liver: EN, enzymology
***Obesity: CO, complications**
Obesity: GE, genetics
Pyruvate Kinase: ME, metabolism
Rats
Rats, Inbred Strains

CAS REGISTRY NO.: 11061-68-0 (Insulin)
CHEMICAL NAME: 0 (Blood **Glucose**); EC 1.1.1.49 (Glucosephosphate Dehydrogenase); EC 2.7.1.2 (Glucokinase); EC 2.7.1.40 (Pyruvate Kinase); EC 3.1.3.11 (Fructose-Bisphosphatase); EC 3.1.3.9 (**Glucose**-6-Phosphatase)

L125 ANSWER 22 OF 76 MEDLINE on STN
ACCESSION NUMBER: 89066780 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2904438
TITLE: High resolution deuterium NMR studies of bacterial metabolism.
AUTHOR: Aguayo J B; Gamcsik M P; Dick J D
CORPORATE SOURCE: Department of Radiology and Radiological Science, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.
CONTRACT NUMBER: EY 0458 (NEI)
SOURCE: The Journal of biological chemistry, **(1988 Dec 25)** Vol. 263, No. 36, pp. 19552-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198901
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 24 Jan 1989

ABSTRACT:
High resolution deuterium NMR spectra were obtained from suspensions of five bacterial strains: Escherichia coli, Clostridium perfringens, Klebsiella pneumoniae, Proteus mirabilis, and Staphylococcus aureus. **Deuterium** -labeled D-**glucose** at C-1, C-2, and C-6 was used to monitor dynamically anaerobic metabolism. The flux of glucose through the various bacterial metabolic pathways could be determined by following the disappearance of glucose and the appearance of the major end products in the 2H NMR spectrum. The presence of both labeled and unlabeled metabolites could be detected using 1H NMR spectroscopy since the proton resonances in the labeled species are shifted upfield due to an isotopic chemical shift effect. The 1H-1H scalar coupling observed in both the 2H and 1H NMR spectra was used to assign definitively the resonances of labeled species. An increase in the intensity

of natural abundance deuterium signal of water can be used to monitor pathways in which a deuteron is lost from the labeled metabolite. The steps in which label loss can occur are outlined, and the influence these processes have on the ability of 2H NMR spectroscopy to monitor metabolism are assessed.

CONTROLLED TERM: *Bacteria: ME, metabolism
Clostridium perfringens: ME, metabolism
Deuterium
Escherichia coli: ME, metabolism
Fermentation
Glucose: ME, metabolism
***Glycolysis**
Kinetics
Klebsiella pneumoniae: ME, metabolism
Magnetic Resonance Spectroscopy: MT, methods
Proteus mirabilis: ME, metabolism
Research Support, U.S. Gov't, P.H.S.
Staphylococcus aureus: ME, metabolism

CAS REGISTRY NO.: 50-99-7 (Glucose); 7782-39-0 (Deuterium)

L125 ANSWER 23 OF 76 MEDLINE on STN
ACCESSION NUMBER: 80197761 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6990920
TITLE: Insulin resistance in soleus muscle from obese Zucker rats. Involvement of several defective sites.
AUTHOR: Crettaz M; Prentki M; Zaninetti D; Jeanrenaud B
SOURCE: The Biochemical journal, **(1980 Feb 15)** Vol. 186, No. 2, pp. 525-34.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198007
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 3 Mar 2000
Entered Medline: 22 Jul 1980
CONTROLLED TERM: Check Tags: Female
Animals
Deoxyglucose: ME, metabolism
Glucose: ME, metabolism
Glycogen: ME, metabolism
Glycolysis
In Vitro
Insulin: ME, metabolism
***Insulin Resistance**
Intracellular Fluid: ME, metabolism
*Muscles: ME, metabolism
***Obesity: ME, metabolism**
Oxygen Consumption
Rats
Receptor, Insulin: ME, metabolism
CAS REGISTRY NO.: 11061-68-0 (Insulin); 154-17-6 (Deoxyglucose); **50-99-7 (Glucose)**; 9005-79-2 (Glycogen)
CHEMICAL NAME: EC 2.7.1.112 (Receptor, Insulin)

L125 ANSWER 24 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 6
ACCESSION NUMBER: 1990:219839 BIOSIS Full-text
DOCUMENT NUMBER: PREV199089117129; BA89:117129
TITLE: CORRECTION OF BA 89016241. IN-VIVO PHOSPHORUS-31 AND

DEUTERIUM NMR STUDIES OF RAT BRAIN TUMOR PH AND BLOOD FLOW DURING ACUTE HYPERGLYCEMIA DIFFERENTIAL EFFECTS BETWEEN SUBCUTANEOUS AND INTRACEREBRAL LOCATIONS. CORRECTION OF TITLE FROM IN-VIVO PHOSPHORUS-31 AND PROTON NMR STUDIES OF RAT BRAIN TUMOR PH AND BLOOD FLOW DURING ACUTE HYPERGLYCEMIA. ERRATUM PUBLISHED IN MAGNETIC RESONANCE MEDICINE VOL. 13. ISS. 1. 1990. P. 175.

AUTHOR(S): ROSS B D [Reprint author]; MITCHELL S L; MERKLE H; GARWOOD M

CORPORATE SOURCE: DEP RADIOL, UNIV MINNESOTA MED SCH, MINNEAPOLIS, MINN 55455, USA

SOURCE: Magnetic Resonance in Medicine, (1989) Vol. 12, No. 2, pp. 219-234.
CODEN: MRMEEN. ISSN: 0740-3194.

DOCUMENT TYPE: Article
Errata

FILE SEGMENT: BA

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 10 May 1990
Last Updated on STN: 10 May 1990

ABSTRACT:Surface coil NMR spectroscopy was used to monitor the hyperglycemia-induced alterations in pH and blood flow in vivo in C6 gliomas implanted both subcutaneously and intracerebrally in rats. Tumor pH was calculated from the chemical shift difference between PCr and Pi in the 31P NMR spectra. Subcutaneous glioma pH decreased 0.8 units by 1 after intraperitoneal administration of an aqueous 50% glucose solution (6 g glucose per kg body weight). In contrast, hyperglycemia failed to significantly alter the pH of intracerebral gliomas which were monitored for 90 min following administration of glucose. Tumor **blood** flow (TBF) was determined both pre- and post-**glucose** administration using **deuterium** NMR by monitoring the time course of D2O washout following intratumoral injection of saline D2O. Subcutaneous and intracerebral TBF were found to have an average change of -78.1% (range -47.4 to -93.3%, n = 5) and -21.1% (range +6.0 to -37.8%, n = 9), respectively. In addition, laser Doppler blood flow measurements of rat skin and subcutaneous glioma revealed a dramatic reduction in blood flow in both tissues following glucose administration. These results indicate that the effects of acute hyperglycemia are site dependent and that hyperglycemia alone is not beneficial for inducing intracellular acidosis in intracerebral tumors.

CONCEPT CODE: Radiation biology - Radiation and isotope techniques 06504
Biochemistry studies - General 10060
Biochemistry studies - Carbohydrates 10068
Biophysics - Methods and techniques 10504
Physiology - Instrumentation 12004
Pathology - Diagnostic 12504
Metabolism - General metabolism and metabolic pathways 13002
Metabolism - Carbohydrates 13004
Metabolism - Metabolic disorders 13020
Cardiovascular system - Physiology and biochemistry 14504
Blood - Blood and lymph studies 15002
Integumentary system - General and methods 18501
Nervous system - General and methods 20501
Nervous system - Pathology 20506
Neoplasms - Diagnostic methods 24001

INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation);
Cardiovascular System (Transport and Circulation);
Equipment, Apparatus, Devices and Instrumentation;

Metabolism; Nervous System (Neural Coordination); Pathology; Tumor Biology

INDEX TERMS: Miscellaneous Descriptors
CORRECTED ARTICLE RAT GLIOMA C6 CELLS INTRACEREBRAL GLIOMA INTRACELLULAR ACIDOSIS TUMOR HEMODYNAMICS DISEASE MONITORING

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 7723-14-0 (PHOSPHORUS-31)
7782-39-0 (DEUTERIUM)

L125 ANSWER 25 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:564596 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100564596
TITLE: Quantitation of tracer levels of deuterium enrichment in all positions of human plasma glucose by 2H NMR.
AUTHOR(S): Jones, J. G. [Reprint author]; Solomon, M. A. [Reprint author]; Sherry, A. D. [Reprint author]; Cao, L. [Reprint author]; Malloy, C. R. [Reprint author]
CORPORATE SOURCE: Mary Nell and Ralph B. Rogers Magnetic Resonance Center, U.T. Southwestern Medical Center, Dallas, TX, USA
SOURCE: Journal of Investigative Medicine, (March, 2000) Vol. 48, No. 2, pp. 192A. print.
Meeting Info.: American Federation for Medical Research Annual Meeting at Experimental Biology 2000. San Diego, California, USA. April 14-18, 2000.
ISSN: 1081-5589.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Dec 2001
Last Updated on STN: 25 Feb 2002
CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520
Radiation biology - General 06502
Biochemistry studies - General 10060
INDEX TERMS: Major Concepts
Chemistry; Methods and Techniques; Radiation Biology
INDEX TERMS: Chemicals & Biochemicals
deuterium: plasma glucose
enrichment, tracer level quantitation; monoacetone derivative of glucose
INDEX TERMS: Methods & Equipment
proton NMR: quantitation method
INDEX TERMS: Miscellaneous Descriptors
investigative medicine; Meeting Abstract
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates,

Vertebrates
REGISTRY NUMBER: 7782-39-0 (deuterium)

L125 ANSWER 26 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:527970 BIOSIS Full-text
DOCUMENT NUMBER: PREV199699250326
TITLE: Noninvasive assessment of the relative roles of cerebral antioxidant enzymes by quantitation of pentose phosphate pathway activity.
AUTHOR(S): Ben-Yoseph, Oded [Reprint author]; Boxer, Peter A.; Ross, Brian D.
CORPORATE SOURCE: Univ. Michigan, 1150 W. Medical Centre Drive, MSRB III, R9303, Box 0648, Ann Arbor, MI 48109-0648, USA
SOURCE: Neurochemical Research, (1996) Vol. 21, No. 9, pp. 1005-1012.
CODEN: NEREDZ. ISSN: 0364-3190.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Nov 1996
Last Updated on STN: 23 Nov 1996

ABSTRACT:Cerebral pentose phosphate pathway (PPP) plays a role in the biosynthesis of macromolecules, antioxidant defense and neurotransmitter metabolism. Studies on this potentially important pathway have been hampered by the inability to easily quantitate its activity, particularly in vivo. In this study we review the use of (1,6-13C-2,6,6-2H-2)glucose for measuring the relative activities of the PPP and **glycolysis** in a single incubation in cultured neurons and in vivo, when combined with microdialysis techniques. PPP activity in primary cerebrocortical cultures and in the caudate putamen of the rat in vivo was quantitated from data obtained by GC/MS analysis of released labeled lactate following metabolic degradation of (1,6-13C-2,6,6-2H-2)glucose. Exposure of cultures to H-2O-2 resulted in stimulation of PPP activity in a concentration-dependent fashion and subsequent cell death. Chelation of iron during H-2O-2 exposure exerted a protective effect thus implicating the participation of the Fenton reaction in mediating damage caused by the oxidative insult. Partial inhibition of glutathione peroxidase, but not catalase, was extremely toxic to the cultures reflecting the pivotal role of GPx in H-2O-2 detoxification. These results demonstrate the ability to dynamically monitor PPP activity and its response to oxidative challenges and should assist in facilitating our understanding of antioxidant pathways in the CNS.

CONCEPT CODE: Biochemistry studies - Carbohydrates 10068
Metabolism - Carbohydrates 13004
Nervous system - Physiology and biochemistry 20504
INDEX TERMS: Major Concepts
Metabolism; Nervous System (Neural Coordination)
INDEX TERMS: Chemicals & Biochemicals
GLUTATHIONE PEROXIDASE
INDEX TERMS: Miscellaneous Descriptors
(1,6-13-CARBON-6,6-**DEUTERIUM**)**GLUCOSE**
; ANALYTICAL METHOD; ANTIOXIDANT PATHWAYS; FETUS; GAS CHROMATOGRAPHY/MASS SPECTROMETRY; GLUTATHIONE PEROXIDASE; METABOLIC DEGRADATION; NERVOUS SYSTEM; NEURON; PENTOSE PHOSPHATE
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat

Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
REGISTRY NUMBER: 9013-66-5 (GLUTATHIONE PEROXIDASE)

L125 ANSWER 27 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:231598 BIOSIS Full-text
DOCUMENT NUMBER: PREV199698795727
TITLE: Effects of fish oil on metabolic responses to oral fructose and glucose loads in healthy humans.
AUTHOR(S): Delarue, Jacques [Reprint author]; Couet, Charles; Cohen, Richard; Brechot, Jean-Francois; Antoine, Jean-Michel; Lamisse, Fernand
CORPORATE SOURCE: Lab. Nutr., Hop. Bretonneau, 37044 Tours, France
SOURCE: American Journal of Physiology, (1996) Vol. 270, No. 2 PART 1, pp. E353-E362.
CODEN: AJPHAP. ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 May 1996
Last Updated on STN: 28 May 1996
ABSTRACT:This study examines the effect of the substitution of 6 g/day of fish oil in a saturated diet on glucose and fructose metabolism in healthy humans. Five subjects were submitted to two 3-wk controlled-diet periods (polyunsaturated/saturated = 0.21). During one period, 6 g/day of fat used for dressing were replaced by 6 g/day of fish oil (1.1 g/day of 20:5 (n-3) fatty acids and 0.7 g/day of 22:6 (n-3) fatty acids). At the end of each period the subjects ingested a 1 g/kg fructose or glucose load 2 days apart. ***Plasma*** glucose fluxes were traced with the use of **deuterated** ***glucose*** and (U-13C)glucose. Substrate oxidation was measured by indirect calorimetry. Fish oil induced a 4% increase in basal and postload glycemia and a 40% decrease in insulinemia, whereas plasma C-peptide remained unaffected. Glucose fluxes were unaffected by fish oil, but carbohydrate (CHO) oxidation was reduced (fructose: 55.5 +- 4.1 vs. 62.9 +- 3.6 g/6 h; glucose: 36.7 +- 4.7 vs. 50.5 +- 4.7 g/6 h; all P lt 0.05). Lipid oxidation was increased 35% by fish oil after both CHO loads. Nonoxidative glucose disposal was increased by fish oil (fructose: 9.4 +- 2.5 vs. 2.9 +- 1.1 g/6 h; glucose: 28.3 +- 5.1 vs. 14.4 +- 4.7 g/6 h; all P lt 0.05). Fish oil could affect glucose transport and decrease CHO oxidation through the decrease in insulinemia and/or a specific effect on glycolytic pathway.
CONCEPT CODE: Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Metabolism - Carbohydrates 13004
Nutrition - Lipids 13222
Food technology - Fats and oils 13514
Food technology - Fish and other marine and freshwater products 13522
Endocrine - Pancreas 17008
INDEX TERMS: Major Concepts
Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Nutrition
INDEX TERMS: Chemicals & Biochemicals
FRUCTOSE; GLUCOSE; INSULIN
INDEX TERMS: Miscellaneous Descriptors
INSULIN; OMEGA-3 FATTY ACIDS
ORGANISM: Classifier
Hominidae 86215

Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Hominidae
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
REGISTRY NUMBER: 57-48-7Q (FRUCTOSE)
30237-26-4Q (FRUCTOSE)
50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)
9004-10-8 (INSULIN)

L125 ANSWER 28 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:179770 BIOSIS Full-text
DOCUMENT NUMBER: PREV199497192770
TITLE: 13C NMR study of the generation of C-2- and C-3-deuterated lactic acid by tumoral pancreatic islet cells exposed to D-(1-13C)-, D-(2-13C)- and D-(6-13C)-glucose in 2H-2O.
AUTHOR(S): Willem, Rudolph; Biesemans, Monique; Kayser, Francois; Malaisse, Willy J. [Reprint author]
CORPORATE SOURCE: Lab. Experimental Med., Erasmus Med. Sch., Brussels Free University, 808 Route de Lennik, B-1070 Brussels, Belgium
SOURCE: Magnetic Resonance in Medicine, (1994) Vol. 31, No. 3, pp. 259-267.
CODEN: MRMEEN. ISSN: 0740-3194.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Apr 1994
Last Updated on STN: 18 Nov 1994
ABSTRACT:Tumoral pancreatic islet cells of the RIN5mF line were incubated for 120 min in media prepared in 2H-2O and containing D-(1-13C)glucose, D-(2-13C)glucose, and D-(6-13C)glucose. The generation of C-2- and C-3-deuterated lactic acid was assessed by 13C NMR. The interpretation of experimental results suggests that a) the efficiency of deuteration on the C-1 of D-fructose 6-phosphate does not exceed about 47% and 4% in the phosphoglucolsomerase and phosphomannolsomerase reactions, respectively; b) approximately 38% of the molecules of D-glyceraldehyde 3-phosphate generated from D-**glucose** escape **deuteration** in the sequence of reactions catalyzed by triose phosphate isomerase and aldolase; and c) about 41% of the molecules of pyruvate generated by **glycolysis** are immediately converted to lactate, the remaining 59% of pyruvate molecules undergoing first a single or double back-and-forth interconversion with L-alanine. It is proposed that this methodological approach, based on high resolution 13C NMR spectroscopy, may provide novel Information on the regulation of back-and-forth interconversion of glycolytic intermediates in intact cells as modulated, for Instance, by enzyme-to-enzyme tunneling.
CONCEPT CODE: Cytology - Animal 02506
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Enzymes - Physiological studies 10808
Anatomy and Histology - Radiologic anatomy 11106
Metabolism - Carbohydrates 13004
Metabolism - Proteins, peptides and amino acids 13012
Digestive system - Pathology 14006
Neoplasms - Biochemistry 24006
Tissue culture, apparatus, methods and media 32500

INDEX TERMS: Major Concepts
Cell Biology; Digestive System (Ingestion and Assimilation); Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Morphology; Tumor Biology

INDEX TERMS: Chemicals & Biochemicals
LACTIC ACID; GLUCOSE; D-FRUCTOSE 6-PHOSPHATE; PHOSPHOGLUCOISOMERASE; PHOSPHOMANNOISOMERASE; D-GLYCERALDEHYDE 3-PHOSPHATE; TRIOSE PHOSPHATE ISOMERASE; ALDOLASE; PYRUVATE; L-ALANINE

INDEX TERMS: Miscellaneous Descriptors
ALDOLASE; D-FRUCTOSE 6-PHOSPHATE; D-GLYCERALDEHYDE 3-PHOSPHATE; L-ALANINE; PHOSPHOGLUCOISOMERASE; PHOSPHOMANNOISOMERASE; PYRUVATE; RAT RIN5MF CELL LINE; TRIOSE PHOSPHATE ISOMERASE

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
Muridae
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 50-21-5 (LACTIC ACID)
50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)
643-13-0 (D-FRUCTOSE 6-PHOSPHATE)
9001-41-6 (PHOSPHOGLUCOISOMERASE)
9023-88-5 (PHOSPHOMANNOISOMERASE)
591-57-1 (D-GLYCERALDEHYDE 3-PHOSPHATE)
9023-78-3 (TRIOSE PHOSPHATE ISOMERASE)
9024-52-6 (ALDOLASE)
57-60-3 (PYRUVATE)
56-41-7 (L-ALANINE)

L125 ANSWER 29 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1993:470416 BIOSIS Full-text
DOCUMENT NUMBER: PREV199345093541
TITLE: Measurement of the pentose phosphate pathway (PPP) in cultured glioma cells in a single incubation using (1,6-carbon-13-2 6,6-**deuterium**-2) **glucose**

AUTHOR(S): Ross, B. D.; Ben-Yoseph, O.
CORPORATE SOURCE: Univ. Michigan, Dep. Radiol., Ann Arbor, MI 48109-0553, USA

SOURCE: Journal of Neurochemistry, (1993) Vol. 61, No. SUPPL., pp. S231.
Meeting Info.: Fourteenth Meeting of the International Society for Neurochemistry. Montpellier, France. August 22-27, 1993.
CODEN: JONRA9. ISSN: 0022-3042.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 1993
Last Updated on STN: 30 Nov 1993

CONCEPT CODE: Cytology - Animal 02506
Cytology - Human 02508
Radiation biology - Radiation and isotope techniques 06504
Biochemistry - Gases 10012

Biochemistry studies - Carbohydrates 10068
Metabolism - Carbohydrates 13004
Nervous system - Pathology 20506
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Biochemistry 24006
Tissue culture, apparatus, methods and media 32500

INDEX TERMS: Major Concepts
Cell Biology; Metabolism; Neurology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences)

INDEX TERMS: Chemicals & Biochemicals
GLUCOSE; CARBON-14 CARBON DIOXIDE; LACTATE

INDEX TERMS: Miscellaneous Descriptors
ABSTRACT; CARBON-14 CARBON DIOXIDE; **GLYCOLYSIS** ; LACTATE; RADIOLABELING

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)
113-21-3 (LACTATE)
51-90-1 (CARBON-14 CARBON DIOXIDE)

L125 ANSWER 30 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1993:470415 BIOSIS Full-text
DOCUMENT NUMBER: PREV199345093540
TITLE: In vivo measurement of the pentose phosphate pathway (PPP) in brain and glioma using a novel precursor: (1,6 carbon-13-2 6,6-**deuterium**-2) **glucose.**
AUTHOR(S): Ben-Yoseph, O. [Reprint author]; Ross, B. D.; Camp, D. M.; Robinson, T. E.
CORPORATE SOURCE: Univ. Michigan, Dep. Radiol., Ann Arbor, MI 48109, USA
SOURCE: Journal of Neurochemistry, (1993) Vol. 61, No. SUPPL., pp. S230.
Meeting Info.: Fourteenth Meeting of the International Society for Neurochemistry. Montpellier, France. August 22-27, 1993.
CODEN: JONRA9. ISSN: 0022-3042.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Oct 1993
Last Updated on STN: 30 Nov 1993
CONCEPT CODE: Cytology - Animal 02506

Biochemistry studies - Lipids 10066
Biochemistry studies - Carbohydrates 10068
Metabolism - Carbohydrates 13004
Metabolism - Lipids 13006
Nervous system - Pathology 20506
Neoplasms - Pathology, clinical aspects and systemic effects 24004
Neoplasms - Biochemistry 24006
Development and Embryology - Morphogenesis 25508

INDEX TERMS: Major Concepts
Cell Biology; Development; Metabolism; Nervous System (Neural Coordination); Tumor Biology

INDEX TERMS: Chemicals & Biochemicals
GLUCOSE

INDEX TERMS: Miscellaneous Descriptors
ABSTRACT; CELL PROLIFERATION; **GLYCOLYSIS**; LIPID SYNTHESIS

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)

L125 ANSWER 31 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:138481 BIOSIS Full-text
DOCUMENT NUMBER: PREV199293072706; BA93:72706
TITLE: TRIMETHYLSILYL-O-METHYLOXIME DERIVATIVES FOR THE MEASUREMENT OF 6 6-**DEUTERATED** D **GLUCOSE** -ENRICHED **PLASMA** SAMPLES BY GAS CHROMATOGRAPHY-MASS SPECTROMETRY.
AUTHOR(S): KURY D [Reprint author]; KELLER U
CORPORATE SOURCE: DEP RES, KANTONSSPITAL BASEL, 4031 BASEL, SWITZERLAND
SOURCE: Journal of Chromatography Biomedical Applications, (1991) Vol. 572, No. 1-2, pp. 302-306.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 12 Mar 1992
Last Updated on STN: 10 May 1992

ABSTRACT:A new method for the determination of the enrichment of [6,6-2H2]-D-glucose in human plasma by gas chromatography-mass spectrometry (GC-MS) is described. (2,3,4,5,6)-Pentakis-O-trimethylsilyl-O-methyloxime-D-glucose is used as a derivative for the GC measurement. Using GC-MS with electron-impact ionization, the enrichment is measured in the single-ion monitoring mode observing the masses m = 319 and 321. In contrast to other methods the use of this glucose derivative reduced the amount of plasma needed from 200 to 10 µl and no chemical ionization equipment is needed for the mass spectrometer.

CONCEPT CODE: Clinical biochemistry - General methods and applications 10006
Biochemistry methods - Carbohydrates 10058
Biochemistry studies - Carbohydrates 10068
Biophysics - Methods and techniques 10504

Metabolism - Carbohydrates 13004
Blood - Blood and lymph studies 15002

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Clinical Chemistry (Allied Medical Sciences); Metabolism; Methods and Techniques

INDEX TERMS: Miscellaneous Descriptors
HUMAN GLUCOSE TURNOVER ANALYTICAL METHOD

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 50-99-7 (D-GLUCOSE)
50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)

L125 ANSWER 32 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1990:334820 BIOSIS Full-text
DOCUMENT NUMBER: PREV199090042839; BA90:42839
TITLE: FLUID AVAILABILITY OF SPORTS DRINKS DIFFERING IN CARBOHYDRATE TYPE AND CONCENTRATION.
AUTHOR(S): DAVIS J M [Reprint author]; BURGESS W A; SLENTZ C A; BARTOLI W P
CORPORATE SOURCE: EXERCISE BIOCHEMISTRY LAB, DEP EXERCISE SCIENCE, UNIVERSITY SOUTH CAROLINA, COLUMBIA, SC 29208, USA
SOURCE: American Journal of Clinical Nutrition, (1990) Vol. 51, No. 6, pp. 1054-1057.
CODEN: AJCNAC. ISSN: 0002-9165.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 24 Jul 1990
Last Updated on STN: 24 Jul 1990

ABSTRACT:Plasma D2O-accumulation profiles (qualitative indices of fluid-absorption rates) were determined in eight subjects after ingestion of 275 mL of five D2O-labeled beverages: a water placebo (W), 6% maltodextrin (6% M), and three solutions containing a 6%, 8%, and 10% glucose-fructose mix (6% GF, 8% GF, and 10% GF). Except for W all beverages contained 20 mmol sodium/L and 3 mmol potassium/L. No differences in plasma D2O accumulation were found. Plasma glucose increased at 20 and 30 min after ingestion of the carbohydrate drinks and returned to baseline (6% GF and 6% M) or below (8% GF and 10% GF) by 60 min. Insulin responded similarly and, except for a slightly lower value at 30 min for 6% GF, no differences were detected. It appears that fluids in drinks containing ≤ 8-10% carbohydrate (simple sugars or maltodextrins) are made available for dilution in body fluids at similar rates and should be similar in replenishing body fluids lost in sweat during exercise.

CONCEPT CODE: Radiation biology - Radiation and isotope techniques 06504
Biochemistry - Physiological water studies 10011
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Biochemistry studies - Minerals 10069
Physiology - Exercise and physical therapy 12010
Metabolism - Carbohydrates 13004

Metabolism - Proteins, peptides and amino acids 13012
Nutrition - General dietary studies 13214
Nutrition - Carbohydrates 13220
Blood - Blood and lymph studies 15002
Blood - Other body fluids 15010
Urinary system - Physiology and biochemistry 15504
Endocrine - Pancreas 17008

INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Nutrition; Physiology; Radiology (Medical Sciences); Urinary System (Chemical Coordination and Homeostasis)

INDEX TERMS: Miscellaneous Descriptors
HUMAN ABSORPTION RATE **DEUTERATED** WATER MALTODEXTRIN **GLUCOSE** FRUCTOSE MIX INSULIN EXERCISE **SWEAT** LOSS REPLENISHING AGENT

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 9050-36-6 (MALTODEXTRIN)
50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)
57-48-7Q (FRUCTOSE)
30237-26-4Q (FRUCTOSE)
9004-10-8 (INSULIN)

L125 ANSWER 33 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1989:221835 BIOSIS Full-text
DOCUMENT NUMBER: PREV198987113452; BA87:113452
TITLE: USE OF DEUTERIUM LABELLED GLUCOSE IN EVALUATING THE PATHWAY OF HEPATIC GLYCOGEN SYNTHESIS.
AUTHOR(S): GOODMAN M N [Reprint author]; MOSUOKA L K; DE ROPP J S; JONES A D
CORPORATE SOURCE: DEP MED, DIV ENDOCRINOL, NUCLEAR MAGNETIC RESONANCE FAC, FAC ADVANCED INSTRUMENTATION, UNIV CALIFORNIA DAVIS, SCH MED, SACRAMENTO, CALIF 95817, USA
SOURCE: Biochemical and Biophysical Research Communications, (1989) Vol. 159, No. 2, pp. 522-527.
CODEN: BBRCA9. ISSN: 0006-291X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 7 May 1989
Last Updated on STN: 7 May 1989

ABSTRACT:Deuterium labelled glucose has been used to study the pathway of hepatic glycogen synthesis during the fasted-refed transition in rats. Deuterium enrichment of liver glycogen was determined using nuclear magnetic resonance as well as mass spectroscopy. Sixty minutes after oral administration of **deuterated glucose** to fasted rats, the portal vein **blood** was fully enriched with **deuterated** ***glucose.*** Despite this, less than half of the glucose molecules incorporated into liver glycogen contained deuterium. The loss of deuterium label from glucose is consistent with hepatic glycogen synthesis by an indirect pathway requiring prior metabolism of glucose. The use of deuterium labelled

glucose may prove to be a useful probe to study hepatic glycogen metabolism. Its use may also find application in the study of liver glycogen metabolism in humans by a noninvasive means.

CONCEPT CODE: Radiation biology - Radiation and isotope techniques 06504
Comparative biochemistry 10010
Biochemistry methods - Carbohydrates 10058
Biochemistry studies - Carbohydrates 10068
Biophysics - Methods and techniques 10504
Biophysics - Molecular properties and macromolecules 10506
Physiology - Comparative 12003
Metabolism - Carbohydrates 13004
Digestive system - General and methods 14001
Digestive system - Physiology and biochemistry 14004

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation); Metabolism; Physiology

INDEX TERMS: Miscellaneous Descriptors
RAT HUMAN NMR MASS SPECTROSCOPY

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 7782-39-0 (DEUTERIUM)
50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)
9005-79-2 (GLYCOGEN)

L125 ANSWER 34 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1985:259603 BIOSIS Full-text
DOCUMENT NUMBER: PREV198579039599; BA79:39599
TITLE: ABNORMAL MEAL CARBOHYDRATE DISPOSITION IN INSULIN-DEPENDENT DIABETES RELATIVE CONTRIBUTIONS OF ENDOGENOUS GLUCOSE PRODUCTION AND INITIAL SPLANCHNIC UPTAKE AND EFFECT OF INTENSIVE INSULIN THERAPY.
AUTHOR(S): PEHLING G [Reprint author]; TESSARI P; GERICH J E; HAYMOND M W; SERVICE F J; RIZZA R A
CORPORATE SOURCE: DEP INTERNAL MED, MAYO CLIN, ROCHESTER, MINN 55905, USA
SOURCE: Journal of Clinical Investigation, (1984) Vol. 74, No. 3, pp. 985-991.
CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

ABSTRACT:Postprandial hyperglycemia in insulin-deficient, insulin-dependent diabetic subjects may result from impaired suppression of endogenous glucose production and/or abnormal disposition of meal-derived glucose. To investigate the relative conditions of these processes and to determine whether 2 wk of near normoglycemia achieved by using intensive insulin therapy could restore the pattern of glucose disposal to normal, meal-related and endogenous rates of glucose appearance were measured isotopically after ingestion of a mixed meal that contained deuterated glucose in 7 lean insulin-dependent and 5 lean nondiabetic subjects. Diabetic subjects were studied once when insulin deficient and again during intensive insulin therapy after 2 wk of near normoglycemia. Total glucose production was determined by using tritiated

glucose and the contribution of meal-related glucose was determined by using the **plasma** enrichment of **deuterated glucose.** The elevated basal and peak postprandial plasma glucose concentrations (252 ± 33 amd 452 ± 31 mg/dl) of diabetic were decreased by intensive insulin therapy to values (82 ± 6 and 193 ± 10 mg/dl, P < 0.01) that approximated those of nondiabetic subjects (93 ± 3 and 140 ± 15 mg/dl, respectively). Total and endogenous rates of glucose appearance (3091 ± 523 and 1814 ± 474 mg/kg per 8 h) in the diabetic subjects were significantly (P < 0.02) greater than those in nondiabetic subjects (1718 ± 34 and 620 ± 98 mg/kg per 8 h, respectively), whereas meal-derived rates of glucose appearance did not differ. Intensive insulin therapy decreased (P < 0.01) both total (1581 ± 98 mg/kg per 8 h) and endogenous (478 ± 67 mg/kg per 8 h) glucose appearance to rates that approximated those observed in the nondiabetic subjects, but did not alter meal-related glucose appearance. Thus, excessive entry of glucose into the peripheral circulation in insulin-deficient diabetic patients after ingestion of a mixed meal resulted from a lack of appropriate suppression of endogenous glucose production rather than impairment of initial splanchnic glucose uptake. Intensive insulin therapy restored postprandial suppression of endogenous glucose production to rates observed in nondiabetic subjects.

CONCEPT CODE: Mathematical biology and statistical methods 04500
Radiation biology - Radiation and isotope techniques 06504
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Pathology - Therapy 12512
Metabolism - Carbohydrates 13004
Metabolism - Proteins, peptides and amino acids 13012
Metabolism - Metabolic disorders 13020
Nutrition - Carbohydrates 13220
Digestive system - General and methods 14001
Blood - Blood and lymph studies 15002
Blood - Lymphatic tissue and reticuloendothelial system 15008
Endocrine - Pancreas 17008
Pharmacology - Drug metabolism and metabolic stimulators 22003
Pharmacology - Clinical pharmacology 22005
Pharmacology - Endocrine system 22016

INDEX TERMS: Major Concepts
Blood and Lymphatics (Transport and Circulation); Endocrine System (Chemical Coordination and Homeostasis); Metabolism; Nutrition; Pharmacology

INDEX TERMS: Miscellaneous Descriptors
HUMAN METABOLIC-DRUG HORMONE-DRUG HYPERGLYCEMIA

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

REGISTRY NUMBER: 9004-10-8 (INSULIN)
50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)

L125 ANSWER 35 OF 76 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1976:98728 BIOSIS Full-text
DOCUMENT NUMBER: PREV197612098728; BR12:98728

TITLE: GLUCOSE PRODUCTION RATES IN INFANCY AND CHILDHOOD.
AUTHOR(S): BIER D M; LEAKE R D; ARNOLD K J; HAYMOND M; GRUENKE L D; SPERLING M A; KIPNIS D M
SOURCE: Pediatric Research, (1976) Vol. 10, No. 4, pp. 405. CODEN: PEREBL. ISSN: 0031-3998.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable
CONCEPT CODE: Biochemistry methods - Carbohydrates 10058
Biochemistry studies - Carbohydrates 10068
Biophysics - Methods and techniques 10504
Movement 12100
Metabolism - Carbohydrates 13004
Blood - Blood and lymph studies 15002
Pediatrics - 25000
Development and Embryology - Pathology 25503
Development and Embryology - Morphogenesis 25508
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Development; Metabolism; Pediatrics (Human Medicine, Medical Sciences)
INDEX TERMS: Miscellaneous Descriptors
ABSTRACT PREMATURE INFANTS ADULTS **BLOOD** **DEUTERIUM** LABELED **GLUCOSE** GAS CHROMATOGRAPHY MASS SPECTROMETRY
ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
REGISTRY NUMBER: 50-99-7Q (GLUCOSE)
58367-01-4Q (GLUCOSE)
7782-39-0 (DEUTERIUM)

L125 ANSWER 36 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003439676 EMBASE Full-text
TITLE: Rapid turnover of T cells in acute infectious mononucleosis.
AUTHOR: Macallan D.C.; Wallace D.L.; Irvine A.J.; Asquith B.; Worth A.; Ghattas H.; Zhang Y.; Griffin G.E.; Tough D.F.; Beverley P.C.
CORPORATE SOURCE: D.C. Macallan, Department of Infectious Diseases, St. George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, United Kingdom. macallan@sghms.ac.uk
SOURCE: European Journal of Immunology, (2003) Vol. 33, No. 10, pp. 2655-2665. .
Refs: 34
ISSN: 0014-2980 CODEN: EJIMAF
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2003
Last Updated on STN: 13 Nov 2003

ABSTRACT: During acute infectious mononucleosis (AIM), large clones of Epstein-Barr virus-specific T lymphocytes are produced. To investigate the dynamics of clonal expansion, we measured cell proliferation during AIM using ***deuterated*** **glucose** to label DNA of dividing cells in vivo, analyzing cells according to CD4, CD8 and CD45 phenotype. The proportion of labeled CD8(+)CD45R0(+)T lymphocytes was dramatically increased in AIM subjects compared to controls (mean 17.5 versus 2.8%/day; p<0.005), indicating very rapid proliferation. Labeling was also increased in CD4(+)CD45R0(+) cells (7.1 versus 2.1%/ day; p<0.01), but less so in CD45RA(+) cells. Mathematical modeling, accounting for death of labeled cells and changing pool sizes, gave estimated proliferation rates in CD8(+)CD45R(+) cells of 11-130% of cells proliferating per day (mean 47%/day), equivalent to a doubling time of 1.5 days and an appearance rate in blood of about 5 x 10(9) cells/day (versus 7 x 10(7) cells/day in controls). Very rapid death rates were also observed amongst labeled cells (range 28-124, mean 57%/day), indicating very short survival times in the circulation. Thus, we have shown direct evidence for massive proliferation of CD8(+)CD45R0(+)T lymphocytes in AIM and demonstrated that rapid cell division continues concurrently with greatly accelerated rates of cell disappearance.

CONTROLLED TERM: Medical Descriptors:
*infectious mononucleosis
***T lymphocyte**
acute disease
turnover time
lymphocyte clone
Epstein Barr virus
lymphocyte proliferation
in vivo study
phenotype
mathematical computing
cell death
cell labeling
cell size
blood cell count
survival time
circulation
cell division
T lymphocyte activation
human
male
female
clinical article
controlled study
adult
article
priority journal
Drug Descriptors:
glucose: EC, endogenous compound
CD4 antigen: EC, endogenous compound
CD8 antigen: EC, endogenous compound
CD45 antigen: EC, endogenous compound

CAS REGISTRY NO.: (glucose) 50-99-7, 84778-64-3

L125 ANSWER 37 OF 76 EMBASE

ACCESSION NUMBER: 2003165104 EMBASE Full-text
TITLE: Estimating average cellular turnover from 5-bromo-2'-deoxyuridine (BrdU) measurements.
AUTHOR: De Boer R.J.; Mohri H.; Ho D.D.; Perelson A.S.

CORPORATE SOURCE: R.J. De Boer, Department of Theoretical Biology, Utrecht University, Padualaan 8, 3584 CH Utrecht, Netherlands. r.j.deboer@bio.uu.nl
SOURCE: Proceedings of the Royal Society of London - Biological Sciences, (22 Apr 2003) Vol. 270, No. 1517, pp. 849-858. Refs: 36
ISSN: 0962-8452 CODEN: PRLBA4
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 9 May 2003
Last Updated on STN: 9 May 2003

ABSTRACT: Cellular turnover rates in the immune system can be determined by labelling dividing cells with 5-bromo-2'-deoxyuridine (BrdU) or ***deuterated*** **glucose** ((2)H-glucose). To estimate the turnover rate from such measurements one has to fit a particular mathematical model to the data. The biological assumptions underlying various models developed for this purpose are controversial. Here, we fit a series of different models to BrdU data on CD4(+) T cells from SIV(-) and SIV(+) rhesus macaques. We first show that the parameter estimates obtained using these models depend strongly on the details of the model. To resolve this lack of generality we introduce a new parameter for each model, the 'average turnover rate', defined as the cellular death rate averaged over all subpopulations in the model. We show that very different models yield similar estimates of the average turnover rate, i.e. ca. 1% day(-1) in uninfected monkeys and ca. 2% day(-1) in SIV-infected monkeys. Thus, we show that one can use BrdU data from a possibly heterogeneous population of cells to estimate the average turnover rate of that population in a robust manner.

CONTROLLED TERM: Medical Descriptors:
*T lymphocyte activation
*lymphocyte proliferation
*cell labeling
compartment model
mathematical analysis
Macaca
Simian immunodeficiency virus
T lymphocyte subpopulation
cell death
article
priority journal
Drug Descriptors:
*broxuridine
CD4 antigen
CAS REGISTRY NO.: (broxuridine) 59-14-3

L125 ANSWER 38 OF 76 EMBASE
ACCESSION NUMBER: 2002436321 EMBASE Full-text
TITLE: In vivo dynamics of t cell activation, proliferation, and death in HIV-1 infection: Why are CD4(+) but not CD8(+) T cells depleted?.
AUTHOR: Ribeiro R.M.; Mohri H.; Ho D.D.; Perelson A.S.
CORPORATE SOURCE: R.M. Ribeiro, Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM 87545, United States. ruy@lanl.gov

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (26 Nov 2002) Vol. 99, No. 24, pp. 15572-15577. .
Refs: 27
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Jan 2003
Last Updated on STN: 3 Jan 2003

ABSTRACT: **Deuterated glucose** labeling was used to measure the in vivo turnover of T lymphocytes. A realistic T cell kinetic model, with populations of resting and activated T cells, was fitted to D-glucose labeling data from healthy and HIV-1-infected individuals before and after antiretroviral treatment. Our analysis highlights why HIV-1 infection, which increases the fraction of both CD4(+) and CD8(+) T lymphocytes that are proliferating (Ki67(+)), leads to CD4 but not CD8 depletion. We find that HIV-1 infection tends to increase the rates of death and proliferation of activated CD4(+) T cells, and to increase the rate at which resting CD4 T cells become activated, but does not increase the fraction of activated CD4(+) T cells, consistent with their preferential loss in HIV-1-infected individuals. In contrast, HIV-1 infection does not lead to an increase in proliferation or death rates of activated CD8(+) T cells, but did increase the fraction of activated CD8(+) T cells, consistent with these cells remaining in an activated state longer and undergoing more rounds of proliferation than CD4(+) T cells. Our results also explain why telomeres shorten in CD8(+) cells, but not in CD4(+) cells of HIV-1-infected patients, compared with age-matched controls.

CONTROLLED TERM: Medical Descriptors:
***T lymphocyte**
*lymphocyte proliferation
*Human immunodeficiency virus infection
in vivo study
measurement
cell kinetics
cell death
telomere
highly active antiretroviral therapy
cell labeling
human
clinical article
controlled study
adult
article
priority journal
Drug Descriptors:
*CD4 antigen: EC, endogenous compound
*CD8 antigen: EC, endogenous compound
glucose
Ki 67 antigen: EC, endogenous compound
CAS REGISTRY NO.: (glucose) 50-99-7, 84778-64-3

ACCESSION NUMBER: 2002177746 EMBASE Full-text
TITLE: Comparison of insulin secretory function in two mouse models with different susceptibility to β-cell

failure.

AUTHOR: Kooptiwut S.; Zraika S.; Thorburn A.W.; Dunlop M.E.; Darwiche R.; Kay T.W.; Proietto J.; Andrikopoulos S.
CORPORATE SOURCE: Dr. S. Andrikopoulos, University of Melbourne, Department of Medicine, Royal Melbourne Hospital, Parkville, Vic. 3050, Australia. sof@unimelb.edu.au

SOURCE: Endocrinology, (2002) Vol. 143, No. 6, pp. 2085-2092. .
Refs: 49
ISSN: 0013-7227 CODEN: ENDOAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Jun 2002
Last Updated on STN: 6 Jun 2002

ABSTRACT: Type 2 diabetes is characterized by a susceptibility to β-cell failure. However, subjects at risk of developing type 2 diabetes, such as those with obesity or a family history of diabetes, have been shown to display hyperinsulinemia. Although this hyperinsulinemia may be an adaptive response to insulin resistance, the possibility that insulin hypersecretion may be a primary defect has not been thoroughly investigated. The DBA/2 mouse is a model of pancreatic islet susceptibility. Unlike the resistant C57BL/6 mouse strain, the DBA/2 mouse islet fails when stressed with insulin resistance or when exposed to chronic high **glucose** concentrations. The aim of this study was to compare insulin secretory function in the DBA/2 and C57BL/6 strains in the absence of insulin resistance or high **glucose.** Insulin secretion was assessed in vivo using the iv **glucose** tolerance test and in vitro using isolated islets in static incubations. It was shown that DBA/2 mice hypersecreted insulin in vivo, compared with C57BL/6 mice, at 1 d and at 4 and 10 wk of age. This hypersecretion was not attributable to insulin resistance (as assessed by the insulin tolerance test) or increased parasympathetic nervous system outflow. Insulin hypersecretion was also demonstrated in vitro. This was associated with higher glycolysis and ***glucose*** oxidation, and elevated activity (but not protein levels) of islet glucokinase and hexokinase. Furthermore, GLUT2 protein levels were higher, which may explain an increase in glucokinase activity in DBA/2 mouse islets. In summary, the DBA/2 mouse, a model of islet failure, has increased ***glucose*** -mediated insulin secretion from a very early age, which is associated with an increase in **glucose** utilization. Further studies will determine whether there is a link between insulin hypersecretion and subsequent β-cell failure.

CONTROLLED TERM: Medical Descriptors:
*insulin release
*pancreas islet beta cell
non insulin dependent diabetes mellitus
disease predisposition
obesity
family history
hyperinsulinemia
insulin resistance
mouse strain
intravenous glucose tolerance test
insulin tolerance test
cholinergic system
glycolysis
glucose oxidation

nonhuman
male
mouse
animal experiment
animal model
controlled study
article
priority journal
Drug Descriptors:
*insulin: EC, endogenous compound
glucose: EC, endogenous compound
glucose: IV, intravenous drug administration
glucokinase: EC, endogenous compound
hexokinase: EC, endogenous compound
glucose transporter 2: EC, endogenous compound
CAS REGISTRY NO.: (insulin) 9004-10-8; (**glucose**) **50-99-7**, 84778-64-3; (glucokinase) 37237-53-9, 9001-36-9; (hexokinase) 9001-51-8; (**glucose** transporter 2) 357693-20-0

L125 ANSWER 40 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2001095725 EMBASE Full-text
TITLE: Treatment of diabetes with vanadium salts: General overview and amelioration of nutritionally induced diabetes in the Psammomys obesus gerbil.
AUTHOR: Shafrir E.; Spielman S.; Nachliel I.; Khamaisi M.; Bar-On H.; Ziv E.
CORPORATE SOURCE: E. Shafrir, Department of Biochemistry, Hadassah University Hospital, Jerusalem 91120, Israel. shafrir@md2.huji.ac.il
SOURCE: Diabetes/Metabolism Research and Reviews, (2001) Vol. 17, No. 1, pp. 55-66. .
Refs: 121
ISSN: 1520-7552 CODEN: DMRRFM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 2001
Last Updated on STN: 29 Mar 2001

ABSTRACT: Background. Numerous investigations have demonstrated the beneficial effect of vanadium salts on diabetes in streptozotocin (STZ)-diabetic rats, in rodents with genetically determined diabetes and in human subjects. The amelioration of diabetes included the abolition of hyperglycemia, preservation of insulin secretion, reduction in hepatic ***glucose*** production, enhanced glycolysis and lipogenesis and improved muscle **glucose** uptake through GLUT4 elevation and translocation. The molecular basis of vanadium salt action is not yet fully elucidated. Although evidence has been provided that the insulin receptor is activated, the possibility exists that cytosolic non-receptor tyrosine kinase, direct phosphorylation of IRS-1 and activation of PI3-K, leading to GLUT4 translocation, are involved. The raised phosphorylation of proteins in the insulin signaling pathway appears to be related to the inhibition of protein tyrosine phosphatase (PTPase) activity by vanadium salts.

CONTROLLED TERM: Medical Descriptors:
*diabetes mellitus: DT, drug therapy

gerbil
psammomys obesus
caloric intake
hyperglycemia
insulin release
liver
gluconeogenesis
glycolysis
lipogenesis
muscle
glucose transport
molecular biology
cytosol
protein phosphorylation
signal transduction
insulin resistance: DT, drug therapy
hyperinsulinemia: DT, drug therapy
glucose clamp technique
glucose tolerance
glucose utilization
nonhuman
rat
animal experiment
animal model
controlled study
article
priority journal
Drug Descriptors:
*vanadyl sulfate: DT, drug therapy
*vanadyl sulfate: PD, pharmacology
***vanadyl sulfate: SC, subcutaneous drug administration**
glucose: EC, endogenous compound
insulin receptor: EC, endogenous compound
protein tyrosine kinase: EC, endogenous compound
protein tyrosine phosphatase: EC, endogenous compound
glucose transporter: EC, endogenous compound
insulin receptor substrate 1: EC, endogenous compound
phosphatidylinositol 3 kinase: EC, endogenous compound
insulin: EC, endogenous compound
phosphoenolpyruvate carboxykinase (GTP): EC, endogenous compound

CAS REGISTRY NO.: (vanadyl sulfate) 14708-82-8, 27774-13-6; (**glucose**) **50-99-7**, 84778-64-3; (protein tyrosine kinase) 80449-02-1; (protein tyrosine phosphatase) 79747-53-8, 97162-86-2; (insulin receptor substrate 1) 175335-32-7; (phosphatidylinositol 3 kinase) 115926-52-8; (insulin) 9004-10-8; (phosphoenolpyruvate carboxykinase (GTP)) 9013-08-5

COMPANY NAME: Sigma (United States)

L125 ANSWER 41 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001020513 EMBASE Full-text

TITLE: Chronic treatment with 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside increases insulin-stimulated **glucose** uptake and GLUT4 translocation in rat skeletal muscles in a fiber type-specific manner.

AUTHOR: Buhl E.S.; Jessen N.; Schmitz O.; Pedersen S.B.; Pedersen O.; Holman G.D.; Lund S.

CORPORATE SOURCE: Dr. S. Lund, Med. Dept. M(Endocrinology/Diabetes), Aarhus University Hospital, Aarhus Kommunehospital, DK-8000 Aarhus C, Denmark. sl@dadlnet.dk

SOURCE: Diabetes, (2001) Vol. 50, No. 1, pp. 12-17. .
Refs: 42
ISSN: 0012-1797 CODEN: DIAEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jan 2001
Last Updated on STN: 25 Jan 2001

ABSTRACT: Recent studies have demonstrated that chronic administration of AICAR (5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside), an activator of the AMP-activated protein kinase, increases hexokinase activity and the contents of total GLUT4 and glycogen in rat skeletal muscles. To explore whether AICAR also affects insulin-stimulated **glucose** transport and GLUT4 cell surface content, Wistar rats were subcutaneously injected with AICAR for 5 days in succession (1 mg/g body wt). Maximally insulin-stimulated (60 nmol/l) **glucose** uptake was markedly increased in epitrochlearis (EPI) muscle (average 63%, P < 0.001, n = 18-19) and in extensor digitorum longus muscle (average 26%, P < 0.001, n = 26-30). In contrast, administration of AICAR did not maximally influence insulin-stimulated **glucose** transport in soleus muscle. Studies of EPI muscle with the 4,4'-0-[2-[2-[2-[2-[2-[6-(biotinylamino)hexanoyl]amino]ethoxy]ethoxy]et hoxy]-4-(1-azi-2,2,2,-trifluoroethyl)benzoyl]amino-1,3-propanediyl]bis-D-mann ose photolabeling technique showed a concomitant increase (average 68%, P < 0.02) in cell surface GLUT4 content after insulin exposure in AICAR-injected rats when compared with controls. In conclusion, 5 days of AICAR administration induces a pronounced fiber type-specific increase in insulin-stimulated **glucose** uptake and GLUT4 cell surface content in rat skeletal muscle with the greatest effect observed on white fast-twitch glycolytic muscles (EPI). These results are comparable with the effects of chronic exercise training, and it brings the AMP-activated protein kinase into focus as a new interesting target for future pharmacological intervention in insulin-resistant conditions.

CONTROLLED TERM: Medical Descriptors:
*insulin sensitivity
***glucose transport**
*protein transport
*drug effect
long term care
enzyme activation
enzyme activity
protein determination
skeletal muscle
hormone action
extensor digitorum longus muscle
soleus muscle
photoaffinity labeling
technique
cell surface
protein localization
fast muscle
glycolysis
exercise

insulin resistance
nonhuman
male
rat
animal experiment
controlled study
animal tissue
article
priority journal
Drug Descriptors:
*5 amino 4 imidazolecarboxamide riboside: PD, pharmacology
***5 amino 4 imidazolecarboxamide riboside: SC, subcutaneous drug administration**
***glucose: EC, endogenous compound**
*insulin: EC, endogenous compound
*protein glut4: EC, endogenous compound
***glucose transporter: EC, endogenous compound**
adenosine phosphate
mannose
4,4' o [2 [2 [2 [2 [2 [6 (biotinylamino)hexanoyl]amino]etho xy]ethoxy]ethoxy]] 4 [[(1 azi 2,2,2, trifluroethyl)benzoyl]amino 1,3 propanediyl]bis dextro mannose
unclassified drug
CAS REGISTRY NO.: (5 amino 4 imidazolecarboxamide riboside) 2627-69-2; (**glucose**) **50-99-7**, 84778-64-3; (insulin) 9004-10-8; (adenosine phosphate) 61-19-8, 8063-98-7; (mannose) 31103-86-3, 3458-28-4
COMPANY NAME: Sigma (United States)

L125 ANSWER 42 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2000279472 EMBASE Full-text
TITLE: Thalidomide impairs insulin action on **glucose** uptake and glycogen synthesis in patients with type 2 diabetes.
AUTHOR: Iqbal N.; Zayed M.; Boden G.
CORPORATE SOURCE: Dr. G. Boden, Temple University Hospital, 3401 N. Broad St., Philadelphia, PA 19140, United States
SOURCE: Diabetes Care, (2000) Vol. 23, No. 8, pp. 1172-1176. .
Refs: 23
ISSN: 0149-5992 CODEN: DICAD2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 31 Aug 2000
Last Updated on STN: 31 Aug 2000
ABSTRACT: OBJECTIVE - To investigate the effect of thalidomide on ***glucose*** turnover (**glucose** production and uptake), on intracellular pathways of **glucose** utilization (glycogen synthesis [GS], glycolysis [GLS], carbohydrate oxidation, and nonoxidative GLS), and on free fatty acid (FFA) turnover (lipolysis, FFA oxidation, and FFA reesterification). RESEARCH DESIGN AND METHODS - A total of 6 patients with type 2 diabetes were studied with 4-h isoglycemic-hyperinsulinemic clamps (.apprx.8 mmol/l and 500-600 pmol/l, respectively) before treatment (Prestudy), after 3 weeks of thalidomide (150 mg orally at bedtime), and after 3 weeks of

placebo. RESULTS - Thalidomide reduced insulin-stimulated **glucose** uptake by 31% (from 27.7 to 19.2 μmol · kg-1 · min-1, P < 0.05) compared with the prestudy and by 21% (from 24.2 to 19.2 μmol · kg-1 · min-1, P < 0.05) compared with placebo. Thalidomide also reduced insulin-stimulated GS by 48% (from 14.1 to 8.2 μmol · kg-1 · min-1, P < 0.05) compared with the prestudy and by 40% (from 13.6 to 8.2 μmol · kg-1 · min-1, P < 0.5) compared with placebo.
Thalidomide had no effect on rates of GLS, carbohydrate oxidation, nonoxidative GLS, lipolysis, FFA oxidation, and reesterification. CONCLUSIONS - We conclude that thalidomide increased insulin resistance in obese patients with type 2 diabetes by inhibiting insulin-stimulated GS and that patients taking thalidomide should be monitored for possible deterioration in their ***glucose*** tolerance.

CONTROLLED TERM: Medical Descriptors:
***glucose transport**
*glycogen synthesis
*non insulin dependent diabetes mellitus: DT, drug therapy
***insulin resistance**
gluconeogenesis
glucose utilization
glycolysis
fatty acid metabolism
lipolysis
oxidation
esterification
human
male
female
clinical article
clinical trial
single blind procedure
crossover procedure
controlled study
adult
article
Drug Descriptors:
*thalidomide: CT, clinical trial
*thalidomide: DT, drug therapy
***thalidomide: PO, oral drug administration**
fatty acid: EC, endogenous compound
glucose: EC, endogenous compound
lactic acid: EC, endogenous compound
alanine: EC, endogenous compound

CAS REGISTRY NO.: (thalidomide) 50-35-1; (**glucose**) **50-99-7**, 84778-64-3; (lactic acid) 113-21-3, 50-21-5; (alanine) 56-41-7, 6898-94-8

L125 ANSWER 43 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1999209940 EMBASE Full-text
TITLE: Effect of reduced inspired oxygen on fetal growth and maternal glucose metabolism in rat pregnancy.
AUTHOR: Saker F.; Voora D.M.; Mahajan S.D.; Kilic I.; Ismail-Beigi F.; Kalhan S.C.
CORPORATE SOURCE: Dr. S.C. Kalhan, Center for Metabolism/Nutrition, MetroHealth Medical Center, Bell Greve Building, 2500 MetroHealth Dr, Cleveland, OH 44109-1998, United States
SOURCE: Metabolism: Clinical and Experimental, (1999) Vol. 48, No.

6, pp. 738-744. .
Refs: 32
ISSN: 0026-0495 CODEN: METAAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
010 Obstetrics and Gynecology
023 Nuclear Medicine
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jul 1999
Last Updated on STN: 8 Jul 1999

ABSTRACT: The effect of prolonged exposure to a reduced fraction of inspired oxygen ([FiO2] 0.17 for 3 days) on maternal glucose kinetics, placental glucose transporters GLUT1 and GLUT3, and fetal growth was examined in rat pregnancy. Arterial and venous catheters were placed 3 days before the study. [3-3H] ***glucose*** tracer and **deuterium** labeling of water were used to measure the rates of glucose turnover and gluconeogenesis (GNG), respectively. Glucose uptake by maternal tissues was measured using [14C]2-deoxyglucose. Exposure to a reduced FiO2 resulted in a significant decrease (mean ± SE) in fetal weight (room air, 4.02 ± 0.04 g; 0.17 FiO2, 3.27 ± 0.6 g, P < .02). There was a significant increase in the maternal-fetal glucose gradient (maternal-fetal glucose ratio: room air, 1.48 ± 0.11; 0.17 FiO2, 2.26 ± 0.24, P < .05), but there was no change in the maternal or fetal blood lactate concentration. No significant change in maternal blood pH was observed; however, a significant decrease in the blood partial pressure of O2 (PO2) occurred (room air, 97 ± 0.5 tort; 0.17 FiO2, 81 ± 1.8) on day 3. There was no change in the rate of turnover of glucose or GNG in the maternal compartment, nor was there any effect on glucose uptake by the maternal tissues. Placental GLUT1 and GLUT3 mRNA were not different in the control or experimental animals. We conclude that a mild reduction in the FiO2 for 3 days in rat pregnancy results in a significant fetal growth restriction that is not related to any observed alteration in maternal glucose metabolism. The lower glucose concentration in the fetal blood may be the consequence of an increase in fetal glucose metabolism, thereby resulting in an increased maternal-fetal gradient of glucose.

CONTROLLED TERM: Medical Descriptors:
*fetus growth
*glucose metabolism
*glucose transport
*oxygen supply
*pregnancy
*fetus hypoxia: DI, diagnosis
disease model
oxygen breathing
gluconeogenesis
glucose oxidation
isotope tracing
fetus weight
lactate blood level
blood pH
blood oxygen tension
glucose utilization
fetus blood
placenta
nonhuman
rat
animal experiment
controlled study

animal tissue
article
priority journal
Drug Descriptors:
*oxygen: EC, endogenous compound
*glucose: EC, endogenous compound
*glucose transporter: EC, endogenous compound
*lactic acid: EC, endogenous compound
*messenger RNA: EC, endogenous compound
*carbon 14

CAS REGISTRY NO.: (oxygen) 7782-44-7; (glucose) 50-99-7, 84778-64-3; (lactic acid) 113-21-3, 50-21-5; (carbon 14) 14762-75-5

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ACCESSION NUMBER: 1999112604 EMBASE Full-text
TITLE: Insulin resistance and impaired insulin secretion due to phosphofructo- 1-kinase-deficiency in humans.
AUTHOR: Ristow M.; Vorgerd M.; Mohlig M.; Schatz H.; Pfeiffer A.
CORPORATE SOURCE: M. Ristow, Joslin Diabetes Center, Research Division, Cell. Mol. Physiol., One Joslin Place, Boston, MA 02215-5397, United States
SOURCE: Journal of Molecular Medicine, (1999) Vol. 77, No. 1, pp. 96-103. .
Refs: 55
ISSN: 0946-2716 CODEN: JMLME8
COUNTRY: Germany
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
006 Internal Medicine
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Apr 1999
Last Updated on STN: 29 Apr 1999

ABSTRACT: The etiology of non-insulin-dependent diabetes mellitus (NIDDM) is usually explained as a combination of peripheral insulin resistance and impaired beta-cell function. Phosphofructo-1-kinase (PFK1) is a rate limiting enzyme in glycolysis, and its muscle subtype (PFK1-M) deficiency leads to an autosomal recessively inherited disorder known as glycogenosis type VII or Tarui's disease. It was evaluated whether PFK1-M deficiency leads to NIDDM- in humans. A core family of four was evaluated for PFK1-M deficiency by DNA- and enzyme-activity-analyses. All members underwent oral and intravenous ***glucose*** tolerance test (oGTT/ivgtt), as well as an insulin sensitivity test (IST) using octreotide. Results: Father (46 years, BMI 22.4 kg/m2) and older son (19 years, BMI 17.8 kg/m5) showed homozygous PFK1-M deficiency, while mother (47 years, BMI 28.4 kg/m5) and younger son (13 years, BMI 16.5 kg/m5) were shown to be heterozygously PFK1-M-deficient on enzyme activity levels. DNA analysis revealed an exon 5-missense-mutation at one allele of all four members, and an exon 22-frameshift-mutation at the other allele of the two homozygously affected individuals. By oGTT the father showed impaired ***glucose*** tolerance, and the mother clinical diabetes. By ivGTT both parents and the older son had a decreased first phase insulin secretion, and a diminished **glucose** disappearance rate. The IST showed marked insulin resistance in both parents and the older son, and moderate resistance in the younger son, previously not described. ConClusion: PFK1-M-deficiency leads to a metabolic state typical for early NIDDM in homozygously affected humans, especially concerning insulin resistance and loss of first phase beta-cell insulin secretion, and may contribute to the manifestation of NIDDM in a

subgroup of patients.

CONTROLLED TERM: Medical Descriptors:
*non insulin dependent diabetes mellitus: ET, etiology
***insulin resistance**
*insulin release
*enzyme deficiency
enzyme activity
enzyme analysis
insulin sensitivity
glucose tolerance
DNA determination
glucose blood level
glycolysis
glucose metabolism
genotype
exon
intron
human
male
female
clinical article
controlled study
school child
adult
oral drug administration
intravenous drug administration
conference paper
Drug Descriptors:
*6 phosphofructokinase: EC, endogenous compound
***glucose: EC, endogenous compound**
CAS REGISTRY NO.: (6 phosphofructokinase) 9001-80-3; (**glucose**) **50-99-7**, 84778-64-3

L125 ANSWER 45 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1998145714 EMBASE Full-text
TITLE: Troglitazone: An antidiabetic agent.
AUTHOR: Chen C.; Frazier J.
CORPORATE SOURCE: J. Frazier, University Health System Consortium, 2001 Spring Road, Oak Brook, IL 60523, United States. frazier@uhc.edu
SOURCE: American Journal of Health-System Pharmacy, (1 May 1998) Vol. 55, No. 9, pp. 905-925. .
Refs: 61
ISSN: 1079-2082 CODEN: AHSPEK
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jun 1998
Last Updated on STN: 4 Jun 1998
ABSTRACT: The pharmacology, pharmacokinetics, clinical efficacy, adverse effects, and dosage and administration of troglitazone are reviewed. Troglitazone is the first oral thiazolidinedione approved for use in treating non-insulin- dependent diabetes mellitus (NIDDM). The drug's mechanism of action has not been fully elucidated. Troglitazone acts as an insulin

sensitizer. Cell-line and animal models indicate that troglitazone may decrease hepatic **glucose** output by decreasing the rate of gluconeogenesis in the liver or by increasing glycolysis. Troglitazone is rapidly absorbed after oral administration, with peak concentration occurring in two to three hours. Food increases absorption by 30-85%. The drug is extensively metabolized in the liver. Troglitazone has been shown to be efficacious in treating NIDDM, both as monotherapy and in combination with oral sulfonylureas. Patients who are obese or who have high fasting plasma insulin levels may derive the greatest benefit. Patients with impaired **glucose** tolerance, syndrome X, polycystic ovary syndrome, gestational diabetes, or Werner's syndrome may also benefit from troglitazone. Adverse effects, including hematologic abnormalities, liver toxicity, and hypoglycemia, have been rare in published trials; no life-threatening effects have been reported thus far. The recommended initial dosage is 200 mg once daily with meals, with an increase to 400 mg daily if satisfactory glycemic control is not achieved after two to four weeks. The average wholesale price is $348 for 100 200-mg tablets and $534 for 100 400- mg tablets. Troglitazone may be an effective agent for treating NIDDM, especially in patients who are obese or who have high fasting plasma insulin levels.

CONTROLLED TERM: Medical Descriptors:
*diabetes mellitus: DT, drug therapy
non insulin dependent diabetes mellitus: DT, drug therapy
insulin sensitivity
gluconeogenesis
glycolysis
drug absorption
drug metabolism
drug efficacy
insulin blood level
hematologic disease: SI, side effect
drug cost
hypoglycemia: SI, side effect
liver toxicity: SI, side effect
insulin resistance
drug antagonism
drug potentiation
oral drug administration
human
review
priority journal
Drug Descriptors:
*troglitazone: AE, adverse drug reaction
*troglitazone: AD, drug administration
*troglitazone: DO, drug dose
*troglitazone: IT, drug interaction
*troglitazone: DT, drug therapy
*troglitazone: PK, pharmacokinetics
*troglitazone: PD, pharmacology
insulin: EC, endogenous compound
sulfonylurea derivative: IT, drug interaction
sulfonylurea derivative: DT, drug therapy
metformin: IT, drug interaction
colestyramine: IT, drug interaction
paracetamol: IT, drug interaction
warfarin: IT, drug interaction
alcohol: IT, drug interaction
terfenadine: IT, drug interaction
oral contraceptive agent: IT, drug interaction
acarbose: DT, drug therapy

acetohexamide: DT, drug therapy
chlorpropamide: DT, drug therapy
glimepiride: DT, drug therapy
glipizide: DT, drug therapy
glibenclamide: DT, drug therapy
tolazamide
tolbutamide

CAS REGISTRY NO.: (troglitazone) 97322-87-7; (insulin) 9004-10-8; (metformin) 1115-70-4, 657-24-9; (colestyramine) 11041-12-6, 58391-37-0; (paracetamol) 103-90-2; (warfarin) 129-06-6, 2610-86-8, 3324-63-8, 5543-58-8, 81-81-2; (alcohol) 64-17-5; (terfenadine) 50679-08-8; (acarbose) 56180-94-0; (acetohexamide) 968-81-0; (chlorpropamide) 94-20-2; (glimepiride) 93479-97-1; (glipizide) 29094-61-9; (glibenclamide) 10238-21-8; (tolazamide) 1156-19-0; (tolbutamide) 473-41-6, 64-77-7

CHEMICAL NAME: (1) Rezulin

COMPANY NAME: (1) Parke davis (United States)

L125 ANSWER 46 OF 76 EMBASE

ACCESSION NUMBER: 1998337179 EMBASE Full-text

TITLE: Actions of the novel oral antidiabetic agent HQL-975 in insulin- resistant non-insulin-dependent diabetes mellitus model animals.

AUTHOR: Ishikawa Y.; Nagumo M.; Saito I.; Ikemoto T.; Takeno H.; Watanabe K.; Tani T.

CORPORATE SOURCE: K. Watanabe, New Drug Research Department, High Quality Life Research Lab., Bio-Medical Division, 5 Hikaridai, Seika-cho, Souraku-gun, Kyoto 619-02, Japan

SOURCE: Diabetes Research and Clinical Practice, (1998) Vol. 41, No. 2, pp. 101-111. .
Refs: 36
ISSN: 0168-8227 CODEN: DRCPE

PUBLISHER IDENT.: S 0168-8227(98)00080-1

COUNTRY: Ireland

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 28 Oct 1998
Last Updated on STN: 28 Oct 1998

ABSTRACT: The hypoglycemic effects of a novel oral antidiabetic agent, HQL-975, were studied in normal rats, streptozotocin-induced diabetic (STZD) rats and genetically insulin-resistant non-insulin-dependent diabetes mellitus (NIDDM) model animals, KK-Ay mice and Zucker diabetic fatty (ZDF) rats. After the dietary administration of HQL-975 to KK-Ay mice, significant decreases in plasma **glucose**, insulin, triglyceride and non-esterified fatty acid levels were observed. The effective dosage of HQL-975 to decrease the plasma ***glucose*** level by 30% was 3.1 mg/kg per day. However, the plasma ***glucose*** level was not altered after the administration of HQL-975 in normal and STZD rats. The results suggest that HQL-975 is more effective against the abnormalities of **glucose** and lipid metabolism of insulin-resistant model animals than in that of normal and insulin-deficient diabetic animals. It is reported that ZDF rats indicate a severely diabetic state as a result of insulin resistance and further the presence of β-cell insulin secretory defects. Here, HQL-975 (1- 30 mg/kg per day for 7 days) was

administered to ZDF rats: slight decreases in the plasma **glucose** (18%) and lipids (41%) levels were observed in the rats given 30 mg/kg. To clarify the action mechanism of HQL-975, we studied the effects of HQL-975 administration on the insulin action of target tissues in KK-Ay mice. After the dietary administration of HQL-975 (0.001, 0.003, 0.010% for 7 days) to KK-Ay mice, hepatic glycolytic and gluconeogenic key enzyme activities were measured. The **glucose** 6-phosphatase activity was decreased (20-40%) as compared with control. The results suggest that HQL-975 enhances the insulin action in hepatic enzyme regulation. To investigate the actions of HQL-975 in peripheral tissues such as muscle and adipose, an in vivo ***glucose*** uptake study using 3H-2-deoxyglucose was performed in KK-Ay mice treated with HQL-975 (0.010% for 7 days). The 2-deoxyglucose uptake of the basal state was not altered, but the insulin-stimulated 2-deoxyglucose uptake in muscle (41-191%) and adipose (46-88%) tissues was increased by the HQL- 975 treatment as compared with control. These results suggest that HQL-975 also enhances the insulin action of peripheral tissues. Based on these findings, HQL-975 is expected to be useful for treatment of insulin-resistant patients with NIDDM.

CONTROLLED TERM: Medical Descriptors:
*non insulin dependent diabetes mellitus: DT, drug therapy
diabetes mellitus: DT, drug therapy
experimental model
hypoglycemia
insulin resistance
lipid metabolism
enzyme activity
glucose blood level
gluconeogenesis
glycolysis
nonhuman
male
rat
animal model
controlled study
oral drug administration
article
Drug Descriptors:
*oral antidiabetic agent: AD, drug administration
*oral antidiabetic agent: AN, drug analysis
*oral antidiabetic agent: DO, drug dose
*oral antidiabetic agent: DT, drug therapy
*hql 975: AD, drug administration
*hql 975: AN, drug analysis
*hql 975: DO, drug dose
*hql 975: DT, drug therapy
deoxyglucose
tritium
insulin: DT, drug therapy
unclassified drug
novolin r40
CAS REGISTRY NO.: (deoxyglucose) 154-17-6; (tritium) 10028-17-8; (insulin) 9004-10-8
CHEMICAL NAME: (1) Novolin r40; Hql 975
COMPANY NAME: (1) Novo nordisk (Denmark)

L125 ANSWER 47 OF 76 EMBASE
ACCESSION NUMBER: 97205615 EMBASE Full-text
DOCUMENT NUMBER: 1997205615

TITLE: In vivo studies of intrahepatic metabolic pathways.
AUTHOR: Beylot M.; Peroni O.; Diraison F.; Large V.
CORPORATE SOURCE: M. Beylot, LPMR, Faculte de Medecine R. Laennec, Rue G. Paradin, 69372 Lyon Cedex 08, France. beylot@laennec.univ-lyon1.fr
SOURCE: Diabetes and Metabolism, (1997) Vol. 23, No. 3, pp. 251-257. .
Refs: 54
ISSN: 0338-1684 CODEN: DIMEFW
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 7 Aug 1997
Last Updated on STN: 7 Aug 1997

ABSTRACT: In vive studies of liver metabolism have long been limited to measurement by the balance technique or isotope dilution method of the amounts of substrates taken up or produced by the liver. New methods, based mainly on the use of stable isotopes, now allow important data to be obtained on intrahepatic metabolic pathways. Nuclear magnetic resonance and chemical biopsy of glucuronic acid by acetaminophen facilitate the study of glycogen metabolism. Chemical biopsies of liver glutamine by phenylacetate and of cytosolic acetylCoA by sulfamethoxazole provide important data respectively on Krebs cycle activity and gluconeogenesis and on lipogenesis and cholesterol synthesis. Mass isotopomer distribution analysis of molecules synthesised during infusion of 13C- labelled precursors allows an estimation of in vive gluconeogenesis as well as cholesterol synthesis and lipogenesis. Finally, these metabolic pathways can be studied through the incorporation of deuterium from **deuterated** water in **glucose**, fatty acids and cholesterol. All these noninvasive techniques allow investigations to be undertaken in human beings to study the nutritional and hormonal regulation of liver metabolism in normal subjects and in pathological situations.

CONTROLLED TERM: Medical Descriptors:
*diabetes mellitus
*gluconeogenesis
*liver metabolism
article
cholesterol synthesis
citric acid cycle
glycogen metabolism
hormonal regulation
human
lipogenesis
nuclear magnetic resonance
nutrition
obesity
stress
Drug Descriptors:
*cholesterol
*glucose
*glucuronic acid
*glutamine
*glycogen
deuterium oxide
fatty acid
paracetamol
phenylacetic acid
CAS REGISTRY NO.: (cholesterol) 57-88-5; (glucose) 50-99-7, 84778-64-3;

(glucuronic acid) 36116-79-7, 576-37-4, 6556-12-3; (glutamine) 56-85-9, 6899-04-3; (glycogen) 9005-79-2; (deuterium oxide) 11105-15-0, 13587-54-7, 7789-20-0; (paracetamol) 103-90-2; (phenylacetic acid) 103-82-2

L125 ANSWER 48 OF 76 EMBASE

ACCESSION NUMBER: 97012778 EMBASE Full-text
DOCUMENT NUMBER: 1997012778
TITLE: Effect of methadone addiction on **glucose** metabolism in rats.
AUTHOR: Sadava D.; Alonso D.; Hong H.; Pettit-Barrett D.
CORPORATE SOURCE: D. Sadava, W.M. Keck Science Center, 925 N. Mills Avenue, Claremont, CA 91711, United States
SOURCE: General Pharmacology, (1997) Vol. 28, No. 1, pp. 27-29. .
Refs: 15
ISSN: 0306-3623 CODEN: GEPHDP
PUBLISHER IDENT.: S 0306-3623(96)00165-6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
040 Drug Dependence, Alcohol Abuse and Alcoholism
052 Toxicology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 15 Feb 1997
Last Updated on STN: 15 Feb 1997

ABSTRACT: Female albino rats were exposed to methadone over a 35-day period by addition of the drug in their drinking water. The final dose of the drug was 1.8 mg/kg body weight per day. After this period, the drug was withdrawn from some animals for 30 days (postexposure). Compared to unexposed controls, serum ***glucose*** levels rose during exposure and returned to control levels postexposure. Oral **glucose** tolerance tests showed impairment in 35-day drug-exposed animals compared to controls and postexposure. The activities of three key enzymes of glycolysis and three key enzymes of gluconeogenesis were measured in liver during and at the end of the exposure period, as well as postexposure. Compared to unexposed controls and postexposure, specific activities of two glycolytic enzymes in livers of exposed animals - hexokinase and phosphofructokinase 1 - were significantly reduced, whereas the activity of a third glycolytic enzyme - pyruvate kinase - was unchanged. The specific activities of two gluconeogenic enzymes - ***glucose*** -6-phosphatase and fructose-1,6-biphosphatase - were significantly elevated in the drug-exposed animals compared to controls, whereas the activity of a third enzyme - phosphoenolpyruvate carboxykinase - was unchanged. These data indicate that methadone addiction produces a mebolic state similar to insulin-resistant diabetes.

CONTROLLED TERM: Medical Descriptors:
***glucose blood level**
***glucose metabolism**
*opiate addiction
animal experiment
animal model
animal tissue
article
controlled study
diabetes mellitus
drug withdrawal

enzyme activity
female
gluconeogenesis
glycolysis
insulin resistance
nonhuman
oral drug administration
oral glucose tolerance test
priority journal
rat
Drug Descriptors:
***glucose: EC, endogenous compound**
*methadone: TO, drug toxicity
6 phosphofructokinase: EC, endogenous compound
fructose bisphosphatase: EC, endogenous compound
glucose 6 phosphatase: EC, endogenous compound
hexokinase: EC, endogenous compound
liver enzyme: EC, endogenous compound
pyruvate kinase: EC, endogenous compound
CAS REGISTRY NO.: (**glucose**) **50-99-7**, 84778-64-3; (methadone) 1095-90-5, 125-56-4, 23142-53-2, 297-88-1, 76-99-3; (6 phosphofructokinase) 9001-80-3; (fructose bisphosphatase) 9001-52-9; (**glucose** 6 phosphatase) 9001-39-2; (hexokinase) 9001-51-8; (pyruvate kinase) 9001-59-6

L125 ANSWER 49 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 96310025 EMBASE Full-text
DOCUMENT NUMBER: 1996310025
TITLE: Biosynthesis of staurosporine: Incorporation of glucose.
AUTHOR: Yang S.-W.; Cordell G.A.
CORPORATE SOURCE: PCR Pharmaceutical Sciences, Medicinal Chem./Pharmacognosy Dept., University of Illinois,Chicago, IL 60612, United States
SOURCE: Journal of Natural Products, (1996) Vol. 59, No. 9, pp. 828-833. .
ISSN: 0163-3864 CODEN: JNPRDF
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 1996
Last Updated on STN: 19 Nov 1996

ABSTRACT: Previously, it was disclosed that tryptophan provides two units of the basic building blocks involved in the biosynthesis of the indolo[2,3-a]carbazole unit of staurosporine (1). In this paper we describe the incorporation of [1-13C]-D-glucose and [U-13C6]-D-glucose into staurosporine, through which it was established that the amino-sugar moiety is derived from glucose, based on the observation of the direct incorporation of uniformly labeled 13C glucose, and that glucose is converted via glycolysis and the shikimic acid pathway to tryptophan and hence into 1. **Deuterium**-labeled **glucose** derivatives, including [6-2H2]-D-glucose, [2-2H]-D-glucose, and [U-2H7]-D-glucose, were used to determine the biogenetic origin of the protons in staurosporine (1). From uniformly **deuterium**-labeled **glucose** up to seven deuterium atoms were incorporated into 1 according to EIMS. Probably, five protons were incorporated into the glycon moiety, and two protons into the aglycon unit based on an analysis of the

1H-NMR spectrum and the fragment peaks in the EIMS.

CONTROLLED TERM: Medical Descriptors:
*cytotoxicity
*drug synthesis
antifungal activity
article
drug isolation
drug purification
glycolysis
streptomyces
thrombocyte aggregation
Drug Descriptors:
*glucose
*staurosporine: DV, drug development
7 hydroxystaurosporine
carbazole derivative
n benzoylstaurosporine
glucose derivative
protein kinase c inhibitor
shikimic acid
staurosporine derivative
tryptophan

CAS REGISTRY NO.: (glucose) 50-99-7, 84778-64-3; (staurosporine) 62996-74-1; (7 hydroxystaurosporine) 112953-11-4; (n benzoylstaurosporine) 120685-11-2; (shikimic acid) 138-59-0; (tryptophan) 6912-86-3, 73-22-3

CHEMICAL NAME: Cgp 41251; Ucn 01; Ucn 02

L125 ANSWER 50 OF 76 EMBASE

ACCESSION NUMBER: 96151328 EMBASE Full-text

DOCUMENT NUMBER: 1996151328

TITLE: Effects of trandolapril and verapamil on **glucose** transport in insulin- resistant rat skeletal muscle.

AUTHOR: Jacob S.; Henriksen E.J.; Fogt D.L.; Dietze G.J.

CORPORATE SOURCE: Department of Physiology, Ina E. Gittings Building, University of Arizona,Tucson, AZ 85721-0093, United States

SOURCE: Metabolism: Clinical and Experimental, (1996) Vol. 45, No. 5, pp. 535-541. .
ISSN: 0026-0495 CODEN: METAAJ

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 4 Jun 1996
Last Updated on STN: 4 Jun 1996

ABSTRACT: We have used an animal model of insulin resistance-the obese Zucker (fa/fa) rat-to test whether oral administration of the non-sulfhydryl-containing angiotensin-converting enzyme (ACE) inhibitor, trandolapril, alone or in combination with the Ca2+-channel blocker, verapamil, can induce a beneficial effect on insulin-stimulated **glucose** transport and metabolism in skeletal muscle. Insulin-stimulated 2-deoxyglucose (2-DG) uptake in the isolated epitrochlearis muscle was less than 50% as great in obese animals compared with lean (Fa/-) controls ($P < .05$), but was significantly improved in the obese group by both short-term (6 hours, +33%) and long-term (14 days, +70%) oral treatment with trandolapril. Verapamil treatment alone

did not alter insulin-stimulated 2-DG uptake in muscle, but simultaneous administration of verapamil and trandolapril resulted in the most pronounced effect on insulin-stimulated 2-DG uptake (+106%). Long-term treatment with trandolapril alone and in combination with verapamil significantly increased muscle glycogen (+26% to 27%), **glucose** transporter GLUT-4 protein (+27% to 31%), and hexokinase activity (+21% to 49%), and decreased plasma insulin levels (-23% to -29%). Muscle citrate synthase activity was enhanced only when trandolapril and verapamil were administered in combination (+24%). We conclude that the long-acting, non-sulfhydryl-containing ACE inhibitor, trandolapril, alone and in combination with the Ca2+-channel blocker, verapamil, can significantly improve insulin-stimulated **glucose** transport activity in skeletal muscle of the insulin-resistant obese Zucker rat, and that this improvement is associated with favorable adaptive responses in GLUT-4 protein levels, glycogen storage, and activities of relevant intracellular enzymes of **glucose** catabolism.

CONTROLLED TERM: Medical Descriptors:
*skeletal muscle
animal model
animal tissue
article
controlled study
drug half life
enzyme activity
female
glucose transport
glycolysis
insulin blood level
insulin resistance
muscle metabolism
nonhuman
oral drug administration
priority journal
rat
Drug Descriptors:
*deoxyglucose
***glucose**
***glucose transporter: EC, endogenous compound**
*glycogen: EC, endogenous compound
*hexokinase: EC, endogenous compound
*insulin
*trandolapril: CB, drug combination
*trandolapril: AD, drug administration
*trandolapril: PK, pharmacokinetics
*trandolapril: DO, drug dose
*trandolapril: CR, drug concentration
*verapamil: CB, drug combination
*verapamil: AD, drug administration
*verapamil: DO, drug dose
citrate synthase: EC, endogenous compound

CAS REGISTRY NO.: (deoxyglucose) 154-17-6; (**glucose**) **50-99-7**, 84778-64-3; (glycogen) 9005-79-2; (hexokinase) 9001-51-8; (insulin) 9004-10-8; (trandolapril) 87679-37-6; (verapamil) 152-11-4, 52-53-9; (citrate synthase) 9027-96-7

COMPANY NAME: Knoll (Germany)

L125 ANSWER 51 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 96121008 EMBASE Full-text

DOCUMENT NUMBER: 1996121008
TITLE: Fatty acids and insulin resistance.
AUTHOR: Boden G.
CORPORATE SOURCE: Temple University Hospital, 3401 N Broad St.,Philadelphia, PA 19140, United States
SOURCE: Diabetes Care, (1996) Vol. 19, No. 4, pp. 394-395. .
ISSN: 0149-5992 CODEN: DICAD2
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 May 1996
Last Updated on STN: 7 May 1996

ABSTRACT: We have demonstrated that physiological elevations in plasma free fatty acid concentrations inhibit insulin-stimulated **glucose** uptake in a dose- dependent manner in normal control subjects and in patients with NIDDM. Two possible mechanisms were identified. 1) a fat-related inhibition of ***glucose*** transport or phosphorylation that appeared after 3-4 h of fat infusion and 2) a decrease in muscle glycogen synthase activity that appeared after 4-6 h fat infusion. We conclude that elevations of plasma FTAs caused insulin resistance and hence may play a significant role in the pathogenesis of insulin resistance in obesity and NIDDM.

CONTROLLED TERM: Medical Descriptors:
***insulin resistance**
*non insulin dependent diabetes mellitus
*obesity
animal model
animal tissue
carbohydrate metabolism
conference paper
enzyme activity
fatty acid oxidation
glucose transport
glycogen synthesis
glycolysis
hormone action
human
human experiment
human tissue
insulin infusion
intravenous drug administration
lipid metabolism
muscle biopsy
nonhuman
rat
Drug Descriptors:
*fatty acid
*insulin
6 phosphofructokinase: EC, endogenous compound
carbohydrate
glucose
glucose 6 phosphate: EC, endogenous compound
glycogen synthase: EC, endogenous compound
heparin
pyruvate dehydrogenase: EC, endogenous compound

triacylglycerol
CAS REGISTRY NO.: (insulin) 9004-10-8; (6 phosphofructokinase) 9001-80-3; (**glucose**) **50-99-7**, 84778-64-3; (**glucose** 6 phosphate) 56-73-5; (glycogen synthase) 9033-05-0; (heparin) 37187-54-5, 8057-48-5, 8065-01-8, 9005-48-5; (pyruvate dehydrogenase) 9014-20-4

L125 ANSWER 52 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 96109033 EMBASE Full-text
DOCUMENT NUMBER: 1996109033
TITLE: Effects of fish oil on metabolic responses to oral fructose and glucose loads in healthy humans.
AUTHOR: Delarue J.; Couet C.; Cohen R.; Brechot J.-F.; Antoine J.-M.; Lamisse F.
CORPORATE SOURCE: Laboratoire de Nutrition, Hopital Bretonneau,37044 Tours, France
SOURCE: American Journal of Physiology - Endocrinology and Metabolism, (1996) Vol. 270, No. 2 33-2, pp. E353-E362. . ISSN: 0193-1849 CODEN: AJPMD
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Apr 1996
Last Updated on STN: 30 Apr 1996

ABSTRACT: This study examines the effect of the substitution of 6 g/day of fish oil in a saturated diet on glucose and fructose metabolism in healthy humans. Five subjects were submitted to two 3-wk controlled-diet periods (polyunsaturated/saturated = 0.21). During one period, 6 g/day of fat used for dressing were replaced by 6 g/day of fish oil [1.1 g/day of 20:5 (n-3) fatty acids and 0.7 g/day of 22:6 (n-3) fatty acids]. At the end of each period the subjects ingested a 1 g/kg fructose or glucose load 2 days apart. Plasma glucose fluxes were traced with the use of **deuterated glucose** and [U- 13C]glucose. Substrate oxidation was measured by indirect calorimetry. Fish oil induced a 4% increase in basal and postload glycemia and a 40% decrease in insulinemia, whereas plasma C-peptide remained unaffected. Glucose fluxes were unaffected by fish oil, but carbohydrate (CHO) oxidation was reduced (fructose: 55.5 ± 4.1 vs. 62.9 ± 3.6 g/6 h; glucose: 36.7 ± 4.7 vs. 50.5 ± 4.7 g/6 b; all $P < 0.05$). Lipid oxidation was increased 35% by fish oil after both CHO loads. Nonoxidative glucose disposal was increased by fish oil (fructose: 9.4 ± 2.5 vs. 2.9 ± 1.1 g/6 h; glucose: 28.3 ± 5.1 vs. 14.4 ± 4.7 g/6 h; all $P < 0.05$). Fish oil could affect glucose transport and decrease CHO oxidation through the decrease in insulinemia and/or a specific effect on glycolytic pathway.

CONTROLLED TERM: Medical Descriptors:
***insulin resistance**
adult
article
calorimetry
fat intake
female
fructose metabolism
glucose metabolism
glucose transport
glycolysis
human
male

normal human
priority journal
Drug Descriptors:
*fish oil
*fructose
*glucose
CAS REGISTRY NO.: (fish oil) 8016-13-5; (fructose) 30237-26-4, 57-48-7, 7660-25-5, 77907-44-9; (glucose) 50-99-7, 84778-64-3

L125 ANSWER 53 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 93163266 EMBASE Full-text
DOCUMENT NUMBER: 1993163266
TITLE: Age-related insulin resistance.
AUTHOR: Couet C.; Delarue J.; Constans T.; Lamisse F.
CORPORATE SOURCE: Lab Nutrition Clinique Medicale A, Hopital Bretonneau, Centre Hospitalier et Universitaire,F-37044 Tours Cedex, France
SOURCE: Hormone Research, (1992) Vol. 38, No. 1-2, pp. 46-50. .
ISSN: 0301-0163 CODEN: HRMRA3
COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Jul 1993
Last Updated on STN: 4 Jul 1993
ABSTRACT: Impaired **glucose** tolerance occurs with age. This impairment is multifactorial including a decrease in insulin-mediated ***glucose*** uptake by peripheral tissues and a delay in insulin-induced suppression of hepatic **glucose** output. A postbinding defect in insulin action such as a reduced capacity to transcribe more **glucose** transporter mRNA and/or a reduced translocation of preformed **glucose** transporters to plasma membrane is incriminated. However, insulin resistance with age is not a constant finding and other mechanism(s) has (have) to be involved in old individuals with impaired **glucose** tolerance and normal tissue insulin sensitivity.

CONTROLLED TERM: Medical Descriptors:
*aging
***insulin resistance**
adult
carbohydrate intolerance: ET, etiology
conference paper
controlled study
dose response
drug binding
enzyme activity
fatty acid blood level
gene expression regulation
gene translocation
gluconeogenesis
glucose metabolism
glucose transport
glucose transport system
human
human cell

human tissue
impaired glucose tolerance: ET, etiology
insulin sensitivity
intravenous drug administration
liver cell membrane
liver metabolism
muscle tissue
oral drug administration
priority journal
rna transcription
Drug Descriptors:
insulin receptor
*insulin: PD, pharmacology
glucose: EC, endogenous compound
glucose transporter: EC, endogenous compound
glycolytic enzyme: EC, endogenous compound
protein tyrosine kinase: EC, endogenous compound
CAS REGISTRY NO.: (insulin) 9004-10-8; (**glucose**) **50-99-7**, 84778-64-3; (protein tyrosine kinase) 80449-02-1

L125 ANSWER 54 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 89273847 EMBASE Full-text
DOCUMENT NUMBER: 1989273847
TITLE: A potent in vivo effect of ciglitazone on muscle insulin resistance induced by high fat feeding of rats.
AUTHOR: Kraegen E.W.; James D.E.; Jenkins A.B.; Chisholm D.J.; Storlien L.H.
CORPORATE SOURCE: Garvan Institute of Medical Research, St Vincent's Hospital, Sydney, NSW 2010, Australia
SOURCE: Metabolism: Clinical and Experimental, (1989) Vol. 38, No. 11, pp. 1089-1093. .
ISSN: 0026-0495 CODEN: METAAJ
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 002 Physiology
003 Endocrinology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 1991
Last Updated on STN: 12 Dec 1991

ABSTRACT: Ciglitazone (5-4-(1-methylcyclohexylmethoxy)benzyl-thiazolidine-2,4-dione) is a hypoglycemic agent, which has been shown to improve blood ***glucose*** levels and in vitro insulin sensitivity in some genetically hyperglycemic rodents. Whether ciglitazone administration prevents the widespread peripheral insulin resistance induced by high fat feeding (HFF) of rats was examined. Insulin action (euglycemic clamp at 150 mU/L insulin, plus 3H-2-deoxyglucose tracer administration) was studied after 3 weeks on diet in control (high carbohydrate fed [HCF]) and HFF rats with or without a ciglitazone gavage (140 mg/kg/d) for six days prior to study. HFF reduced the ***glucose*** infusion rate required to maintain euglycemia to 57% of control ($P < .01$), but this was restored to 82% of control by ciglitazone treatment ($P < .01$ v HFF alone). Estimated **glucose** disposal (Rd) and skeletal muscle **glucose** metabolic index (Rg', from accumulation of phosphorylated deoxyglucose) were reduced by HFF but restored to control values by concomitant ciglitazone treatment. Ciglitazone increased muscle Rg' by approximately twofold v HFF in all eight muscles sampled. However, in other tissues (white and brown adipose tissue, lung, and heart), ciglitazone did not alter responses from HFF alone. Thus, ciglitazone counteracts whole body

insulin resistance in the HFF rat model mainly due to potent effects on insulin action in both oxidative and glycolytic skeletal muscle.

CONTROLLED TERM: Medical Descriptors:
*adipose tissue
*carbohydrate diet
*fat intake
***glycolysis**
*heart
***insulin resistance**
*lung
*metabolism
*muscle
rat
controlled study
animal experiment
animal cell
nonhuman
male
oral drug administration
priority journal
Drug Descriptors:
radioisotope
*ciglitazone
***glucose**

CAS REGISTRY NO.: (ciglitazone) 74772-77-3; (**glucose**) **50-99-7**, 84778-64-3

COMPANY NAME: Upjohn (United States)

L125 ANSWER 55 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 85200432 EMBASE Full-text

DOCUMENT NUMBER: 1985200432

TITLE: Effect of a novel thermogenic β-adrenoceptor agonist (BRL 26830) on insulin resistance in soleus muscle from obese Zucker rats.

AUTHOR: Challiss R.A.J.; Budohoski L.; Newsholme E.A.; et al.

CORPORATE SOURCE: Department of Biochemistry, University of Oxford, Oxford, OX1 3QU, United Kingdom

SOURCE: Biochemical and Biophysical Research Communications, (1985) Vol. 128, No. 2, pp. 928-935. .
CODEN: BBRCA

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index
008 Neurology and Neurosurgery
029 Clinical Biochemistry
003 Endocrinology

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Dec 1991
Last Updated on STN: 10 Dec 1991

ABSTRACT: Young lean (Fa/?) and obese (fa/fa) rats were treated with the thermogenic β-adrenoceptor agonist, BRL 26830, for 3 weeks. In lean rats this treatment had no effect on body weight but there was a marked increase in the insulin sensitivity of soleus muscle strips with respect to glycolytic rate. Treatment of obese rats with BRL 26830 produced a small but not significant decrease in body weight but the sensitivity of both glycolysis and glycogen synthesis to insulin was increased so that muscles of treated obese rats showed similar insulin sensitivity to untreated lean rats. It is suggested that such changes are unlikely to be merely a secondary consequence

of an anti-obesity action.

CONTROLLED TERM: Medical Descriptors:
*body weight
*drug mechanism
*drug metabolism
*drug sensitivity
***glucose blood level**
***glycolysis**
***insulin resistance**
*muscle
*obesity
glucose c 14
priority journal
intravenous drug administration
normal value
animal experiment
animal cell
animal model
therapy
nonhuman
rat
blood and hemopoietic system
Drug Descriptors:
*4 [2 [(2 hydroxy 2 phenylethyl)amino]propyl]benzoic acid
*beta adrenergic receptor stimulating agent
*insulin
radioisotope
4 [2 [(2 hydroxy 2 phenylethyl)amino]propyl]benzoic acid methyl ester
neutral insulin
CAS REGISTRY NO.: (4 [2 [(2 hydroxy 2 phenylethyl)amino]propyl]benzoic acid) 90730-94-2; (insulin) 9004-10-8; (4 [2 [(2 hydroxy 2 phenylethyl)amino]propyl]benzoic acid methyl ester) 77955-41-0; (neutral insulin) 9004-14-2
CHEMICAL NAME: Brl 26830; Actrapid
COMPANY NAME: Novo

L125 ANSWER 56 OF 76 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 75010489 EMBASE Full-text
DOCUMENT NUMBER: 1975010489
TITLE: Impairment of induction of glycolytic enzymes and development of insulin resistance in rats as a result of continuous insulin treatment.
AUTHOR: Salganik R.I.; Mertvetsov N.P.; Gordienko O.E.; et al.
CORPORATE SOURCE: Inst. Cytol. Genet., Siberian Branch USSR Acad. Sci., Novosibirsk, Russia
SOURCE: Acta Endocrinologica, (1974) Vol. 76, No. 2, pp. 319-331. CODEN: ACENA7
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
030 Pharmacology
003 Endocrinology
023 Nuclear Medicine
LANGUAGE: English
ABSTRACT: It was established that administration of insulin to rats for 10 days results in a considerable increase of RNA synthesis and of the activity of hexokinase and pyruvate kinase in liver cells. Electron microscopic studies showed that on the 6th day of insulin treatment the size of liver cell nucleoli

and the number of free ribosomes increase. On the 10th day of treatment the glycogen content is changed in the liver cells. Following longterm insulin treatment (16-20 days) the liver cells lose their capacity to respons by enhanced RNA synthesis and by the induction of hexokinase and pyruvate kinase. It was also demonstrated that insulin administration for 10-15 days significantly decreases blood sugar. However, continuous insulin treatment (up to 25-27 days) elevates blood sugar to values surpassing even the normal value on day 27 of treatment.Administration of insulin to rats for 25-27 days leads to a decreased tolerance to **glucose** load. The content of immunoreactive insulin in the blood plasma increases considerably on day 10 of insulin injection and continues to rise more sharply on subsequent days of treatment.

CONTROLLED TERM: Medical Descriptors:
*adenine c 14
***glucose blood level**
*nucleolus
*drug resistance
*electron microscopy
*enzyme induction
***glucose tolerance test**
***glycolysis**
***insulin resistance**
*liver
*liver cell
*radioactivity
*rat
*ribosome
*serum
intraperitoneal drug administration
drug blood level
methodology
theoretical study
drug administration
drug analysis
Drug Descriptors:
*adenine
*carbohydrate
***glucose**
***glycolytic enzyme**
*hexokinase
*hydrocortisone
*immunoreactive insulin
*insulin i 125
*isophane insulin
*nucleic acid
*pyruvate kinase
*rna
radioisotope

CAS REGISTRY NO.: (adenine) 22177-51-1, 2922-28-3, 73-24-5; (**glucose**) **50-99-7**, 84778-64-3; (hexokinase) 9001-51-8; (hydrocortisone) 50-23-7; (isophane insulin) 9004-17-5; (pyruvate kinase) 9001-59-6; (rna) 63231-63-0

COMPANY NAME: Orfass (Russia); Isotope (Russia); Richter (Hungary)

L125 ANSWER 57 OF 76 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
DUPLICATE 1

ACCESSION NUMBER: 2006-344255 [35] WPIX
DOC. NO. CPI: C2006-113045 [35]
DOC. NO. NON-CPI: N2006-291734 [35]
TITLE: Method to identify glucose metabolic product comprises administering D7 **glucose**, allowing the **glucose** to form **deuterated** target metabolite, contacting the metabolite with mass tag to form tagged metabolite and detecting the mass
DERWENT CLASS: B04; D16; S03
INVENTOR: HALL M; SCHNEIDER L V; HALL M P
PATENT ASSIGNEE: (TARG-N) TARGET DISCOVERY INC
COUNTRY COUNT: 111

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006050130	A2	20060511	(200635)*	EN	71[0]	
US 20060120961	A1	20060608	(200639)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006050130	A2	WO 2005-US39017	20051028
US 20060120961	A1 Provisional	US 2004-623521P	20041029
US 20060120961	A1	US 2005-262311	20051028

PRIORITY APPLN. INFO: US 2004-623521P 20041029
US 2005-262311 20051028
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0049-00 [I,A]; G01N0033-00 [I,A]
BASIC ABSTRACT:

WO 2006050130 A2 UPAB: 20060602

NOVELTY - Identifying a glucose metabolic product (I), comprising administering a D7 glucose (A), allowing (A) to be at least partially metabolized to form a deuterated target metabolite (B), separating (B) from the subject, contacting (B) with a mass tag and allowing the mass tag to attach to (B) to form a mass tagged deuterated target metabolite and detecting the mass of the mass tagged deuterated target metabolite to identify (I), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) analyzing metabolic pathways (II), comprising: administering a substrate (where the relative isotopic abundance of the isotope in the substrate is known), allowing the labeled substrate to be at least partially metabolized to form one or more target metabolites, and determining the abundance of the isotope in a plurality of target analytes in a sample from the subject to determine a value for the flux of each target analyte, where the plurality of target analytes comprise the substrate and/or one or more of the target metabolites;

(2) screening for metabolites correlated with a disease or cellular state, comprising administering to a test subject and a control subject a substrate and the test subject has the disease, allowing the labeled substrate to be partially metabolized (where the conditions under which the administering and allowing steps are performed are the same for the test and control subject) and obtaining a sample from the test and control subject, determining for each sample the relative abundance of the isotope in a plurality of target analytes and comparing the values for flux for the test and control subjects a difference in the flux value for a target analyte in

the test subject and corresponding flux value for the control subject indicating that such analyte is potentially correlated with the disease;

(3) screening for metabolites correlated with a disease comprises: analyzing a sample from a test subject having the disease and determining the isotopic abundance of the isotope in a plurality of analytes in the sample to determine a value for the flux of each analyte and comparing flux values for the analytes with flux values for the same analytes obtained for a control subject;

(4) screening for the presence of a disease, comprising administering to a test subject a substrate, allowing sufficient time for the labeled substrate to metabolized, performing a plurality of electrophoretic methods in series to at least partially separate a plurality of target analytes from other biological components in a sample obtained from the test subject, determining a flux value for the target analytes, the flux value for each target analyte being determined from the abundance of the isotope in that analyte and comparing determined flux values with corresponding reference flux values for the same target analytes to assess the test subject's risk of disease; and

(5) analyzing metabolites in an initial sample, comprising performing a plurality of capillary electrophoresis methods in series, each method comprising electrophoresing a sample containing multiple metabolites, to obtain a plurality of resolved metabolites (where the sample electrophoresed contains only a subset of the plurality of resolved metabolites from the immediately preceding method in the series, except the first method of the series in which the sample is the initial sample, the metabolites in the initial sample potentially containing one or more target analytes, the capillary electrophoresis methods) and analyzing fractions containing resolved metabolites from the final electrophoretic method to detect the presence of the target analytes.

USE - The method is useful forntifying a glucose metabolic product; and analyzing metabolic pathways. The method is useful forscreening for metabolites correlated with a disease (cancer, autism, microbial infection and digestive disorders) or cellular state (all claimed).

The method is useful to detect a plurality of mass tagged deuterated metabolites; and determine the effect of chemical agents or combination of agents generally have no metabolism and the effect on the flux of certain metabolites of interest.

ADVANTAGE - The method reduce sample amount requirements and analysis time by eliminating multiple steps relative to the known method. The method provides determination of the sequence and the branching structure of a glycoform simulataneously. MANUAL CODE: CPI: B04-B01B; B04-B03A; B04-B03B; B04-B04B; B04-B04D5;

B04-B04G; B04-B04H; B04-C02; B04-D01; B04-E01; B04-F01; B04-N04; B04-N06; B11-C07B5; B11-C08A; B11-C08D1; B11-C10; B12-K04A; D05-H09

EPI: S03-E03E; S03-E14H

TECH

BIOLOGY - Preferred Components: The subject is a mammal or a cell. The sample is obtained from a bodily fluid, the bodily fluid are blood, urine, cerebral fluid, spinal fluid, sweat or gastrointestinal fluids. The sample is a cell, a tissue sample or fecal material.

ORGANIC CHEMISTRY - Preferred Components: (B) is a deuterated monosaccharide or deuterated glycan. The mass tag is a mass defect tag comprising a mass defect element having an atomic number 17-77. The deuterated glycan forms part of a glycoprotein. The mass defect element is bromine or iodine. The mass defect tag comprises at least two mass defect elements having an atomic number 17-77. The one or more target analytes are labeled with an hydrogen isotopic label. The performing of the capillary electrophoresis methods comprises performing a plurality of capillary zone electrophoresis methods. The performing of the capillary

electrophoresis methods generates separate fractions for at least one class of metabolite. The plurality of target analytes comprises the substrate and at least one (preferably 5) target metabolite. The determination of the abundance of the isotope is performed by mass spectrometry (preferred), infrared spectrometry or nuclear magnetic resonance spectrometry. The analyzing is performed by mass spectroscopy, infrared spectroscopy or nuclear magnetic resonance spectroscopy. The class of metabolite/target analytes is proteins, polysaccharides, carbohydrates, nucleic acids, amino acids, nucleotides, nucleosides, fats, fatty acids or organic acids. The target analyte is a glycoprotein. Preferred Method: The mass tag is attached at the reducing end of the deuterated glycan to form a mass tagged deuterated glycan. The method further comprises: fragmenting the mass tagged deuterated glycan, before the step of contacting, using an enzymatic, chemolytic or mass spectrometric fragmentation method to produce a population of labeled mass tagged deuterated glycan fragments and unlabeled deuterated glycan fragments; distinguishing the mass of the labeled mass tagged deuterated glycan fragment and a different molecule having the same number of nucleons as the labeled mass tagged deuterated glycan fragment; and separating the deuterated glycan or a portion of the deuterated glycan from the glycoprotein before the detecting step. The identity of at least one or two monosaccharide at the reducing end of the glycan is determined. The quantity of the mass tagged deuterated target metabolite is determined. In the method, at least two-labeled mass tagged deuterated glycan fragments are detected. The separating step comprises collecting a sample comprising the deuterated target metabolite from the subject and subjecting the sample to a liquid chromatographic procedure to separate the deuterated target metabolite from a sample component.
In (II), the determining step comprises: at least partially separating the target analytes from other biological components in the sample prior to determining the flux values; obtaining multiple samples from the subject at different predetermined time points, separating the target analytes from other biological components in each of the samples and determining the abundance of the isotope in the target analytes contained in each sample (where a plurality of values for the abundance of the isotope in each target analyte are obtained) the flux value for each target analyte being determined from the plurality of abundance values determined for it; and performing a plurality of capillary electrophoresis methods followed by mass spectrometery. In (II), the separating step comprises: performing a plurality of capillary electrophoresis methods in series; and conducting a non-electrophoretic separation technique prior to conducting the plurality of electrophoresis methods to precipitate at least some of the biological components. In the method of screening the separating step comprises performing a plurality of capillary electrophoresis in series with the samples from the test and control subjects. The plurality of capillary electrophoresis methods is capillary zone electrophoresis, capillary isoelectric focusing (both preferred) or capillary gel electrophoresis. In the method of screening, for the presence of disease where: if the reference flux values are representative of presence and/or susceptibility to the disease, a statistically significant difference between reference values and test values indicates that the test subject does not have and/or is not susceptible to acquiring the disease; and if the reference flux values are representative of absence and/or lack of susceptibility to the disease, a statistically significant difference between reference and test values indicates that the test subject does have, or is susceptible to acquiring, the disease. The analyzing step comprises detecting the abundance of the label in each target analyte present.

ACCESSION NUMBER: 2004-238767 [22] WPIX
DOC. NO. CPI: C2004-093427 [22]
DOC. NO. NON-CPI: N2004-189270 [22]
TITLE: Diagnosis of diabetes mellitus and treatment of hyperglycemia involves administration of labeled glucose molecules; quantification of glucose flux and glucose recycling and comparison of the quantified glucose flux with standard
DERWENT CLASS: B04; P31; S03
INVENTOR: KURLAND I J; LEE P W N; LEE W N P; SAAD M; XU J
PATENT ASSIGNEE: (KURL-I) KURLAND I J; (LEEW-I) LEE W N P; (SAAD-I) SAAD M; (REGC-C) UNIV CALIFORNIA; (XUJJ-I) XU J
COUNTRY COUNT: 103

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004016156	A2	20040226	(200422)*	EN	43[10]	A61B000-00
AU 2003265448	A1	20040303	(200457)	EN		
US 20050238581	A1	20051027	(200571)	EN		A61K049-00
AU 2003265448	A8	20051103	(200629)	EN		A61K049-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004016156	A2	WO 2003-US25606	20030816
US 20050238581	A1 Provisional	US 2002-404255P	20020816
AU 2003265448	A1	AU 2003-265448	20030816
US 20050238581	A1 Cont of	WO 2003-US25606	20030816
US 20050238581	A1	US 2005-60640	20050216
AU 2003265448	A8	AU 2003-265448	20030816

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003265448	A1	Based on	WO 2004016156	A
AU 2003265448	A8	Based on	WO 2004016156	A

PRIORITY APPLN. INFO: US 2002-404255P 20020816
WO 2003-US25606 20030816
US 2005-60640 20050216
INT. PATENT CLASSIF.:
MAIN: A61K049-00; A61B
SECONDARY: C12Q001-54; G01N033-00; G01N033-53; G01N037-00
BASIC ABSTRACT:
WO 2004016156 A2 UPAB: 20060121
NOVELTY - Diagnosing diabetes mellitus comprising:
(a) administering several labeled glucose molecules;
(b) quantifying the glucose flux and glucose recycling over time after the administration; and
(c) comparing the quantified glucose flux and recycling with standard to assess the status of the health of the patient, is new.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for screening drug candidates for biological activity for potential use in treating a hyperglycemic patient involving:
(a) labeling at least one carbon atom of a glucose molecule;

(b) introducing labeled glucose molecules and the candidate drug into a mammalian test subject;

(c) determining the rate of glucose flux through metabolic pathways in the liver and the peripheral muscles; and

(d) comparing determined flux rates with known baseline flux rates in the absence of the candidate drug.

ACTIVITY - Antidiabetic.

No biological data given.

MECHANISM OF ACTION - None given.

USE - The methods are useful for diagnosis of diabetes mellitus, for screening drug candidates for biological activity for potential use in treating hyperglycemic patients (claimed), for treating physiological and pathophysiological conditions e.g. hyperglycemia.

ADVANTAGE - The process differentiates between hepatic and peripheral insulin sensitivity and provides diagnostic test for diabetes and other conditions producing hyperglycemia. The process correlates insulin action with the activity of genes thought to be associated with diabetes. The method allows correlation of gene activity, hormone and metabolite levels with glucose flux and recycling and an assessment of degree of hepatic insulin resistance. The method utilizes non-radioactive stable labeled glucose and provides hepatic recycling constant to measure relative rate of glucose recycling. MANUAL CODE: CPI: B04-J03A; B10-A07; B11-C07B5; B11-C08E2; B11-C10; B12-K04A; B12-K04E; B14-S04

EPI: S03-E14A1; S03-E14H

TECH

PHARMACEUTICALS - Preferred Process: The diagnosing method further involves measuring insulin levels at time points after the administration of labeled glucose to the patient; and correlating the insulin level with the quantified glucose flux and glucose recycling. The labeling involves labeling a first carbon of the glucose at a first end of the glucose molecule; and labeling a second carbon in the glucose molecule. The screening process further involves:

(a) measuring hormone and metabolite levels of the test subject;

(b) comparing the levels with known baseline levels of the hormone and metabolites in the absence of the candidate drug;

(c) measuring insulin levels at time points after introduction of labeled glucose into the test subject;

(d) correlating the insulin levels with the rates of glucose flux in the presence of the candidate drug; and comparing the measured insulin levels with the insulin levels observed in the absence of the candidate drug;

(e) collecting array of measurements of flux rates, insulin, hormones and metabolite concentrations from several healthy individuals;

(f) collecting an array of measurements of flux rates, insulin, hormones and metabolite concentrations from several individuals with diagnosed hyperglycemia;

(g) comparing the measurements of flux rates, insulin, hormones and metabolite concentrations from the test subject with the array measurements from healthy individuals and the array of measurements from individuals diagnosed with hyperglycemia;

(h) monitoring glucose flux and recycling levels at different concentration levels of candidate drug to determine a minimum effective dose of candidate drug; and

(i) determining the rate of glucose recycling through metabolic pathways in the liver and the peripheral tissues.

ORGANIC CHEMISTRY - Preferred Components: The labeled first carbon is the first carbon to be metabolized during glucose metabolism. The label comprises a non-radioactive isotope of carbon. The non-radioactive isotope of carbon comprises a 13C isotope. The first carbon and second carbon are either both labeled with non-radioactive isotope of carbon; or are labeled with deuterium marker; or the first carbon is labeled with non-radioactive

isotope of carbon and the second carbon is labeled with **deuterium** marker. The label of the **glucose** comprises (1,213C2)-glucose.

L125 ANSWER 59 OF 76 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-812970 [76] WPIX
DOC. NO. CPI: C2003-226099 [76]
TITLE: Separation of stem cells, useful e.g. for identifying carcinogens and therapeutic agents, by specific labeling of mixed cell populations then separation of labeled cells
DERWENT CLASS: B04; D16
INVENTOR: HELLERSTEIN M K; KIM S J
PATENT ASSIGNEE: (HELL-I) HELLERSTEIN M K; (KIMS-I) KIM S J; (REGC-C) UNIV CALIFORNIA
COUNTRY COUNT: 102

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003087314	A2	20031023	(200376)*	EN	62[10]	C12N000-00
US 20030224420	A1	20031204	(200380)	EN		C12Q001-68
AU 2003234688	A1	20031027	(200436)	EN		
TW 2004001826	A	20040201	(200568)	ZH		C12N015-00
AU 2003234688	A8	20051110	(200634)	EN		C12Q001-68

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003087314	A2	WO 2003-US10554	20030404
US 20030224420	A1 Provisional	US 2002-370599P	20020405
AU 2003234688	A1	AU 2003-234688	20030404
US 20030224420	A1	US 2003-407435	20030404
TW 2004001826	A	TW 2003-107883	20030407
AU 2003234688	A8	AU 2003-234688	20030404

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2003234688	A1	Based on	WO 2003087314	A
AU 2003234688	A8	Based on	WO 2003087314	A

PRIORITY APPLN. INFO: US 2002-370599P 20020405
US 2003-407435 20030404
INT. PATENT CLASSIF.:
MAIN: C12N015-00; C12Q001-68; C12N
SECONDARY: C12N005-08; G01N033-53; G01N033-567; G01N033-574; C12P019-34; C12Q001-00

BASIC ABSTRACT:

WO 2003087314 A2 UPAB: 20060120

NOVELTY - Method for separating stem cells (SC) from a tissue or individual.

DETAILED DESCRIPTION - Method for separating stem cells (SC) from a tissue or individual comprises:

(a) administering at least one cell-lineage marker label (L) such that these are incorporated into cells;

(b) stopping the administration so that a population of cells (P2) with detectably higher L content, relative to another population (P1), is formed; and

(c) detecting the presence/amount of L in both populations, then separating P2 as SC.

INDEPENDENT CLAIMS are also included for the following:

(1) identifying carcinogenesis by separating SC by the new method and detecting any carcinogenesis-related DNA modifications in them;

(2) identifying a chemical as genotoxic by administering a test compound, separating SC by the new method and detecting a DNA modification;

(3) identifying a phenotypic marker of SC comprising separating SC by the new method and comparing its phenotype with that of non-stem cells;

(4) determining SC proliferation;

(5) identifying therapeutic compounds from their effect on SC proliferation;

(6) identifying a compound that stimulates SC proliferation; and

(7) kits for separating SC or for determining their proliferation rate.

USE - The separated stem cells (SC) are used:

(i) to identify carcinogenesis and agents that are genotoxic;

(ii) to identify phenotypic markers of SC;

(iii) to measure the proliferation rate of SC, particularly for identifying therapeutic agents, stimulators of SC proliferation and diagnosis of disease such as diabetes (testing beta-cells), immunodeficiency, particularly HIV infection (testing T lymphocytes) or guest versus host diseases (testing bone marrow cells) (claimed),

They are also used for monitoring:

(a) treatment of cancer or the risk of developing it;

(b) response of T cells to antigenic stimulation (testing efficacy of vaccines);

(c) spermatogenesis and adipogenesis; and

(d) maintenance of epithelial cell populations. MANUAL CODE:

CPI: B04-B03B; B04-F02; B04-F0200E; B11-C08A; B12-K04; B12-K04E; D05-H08; D05-H13

TECH

BIOLOGY - Preferred Materials: L is a halogenated deoxyribonucleotide, specifically bromo- or iodo-deoxyuridine. The tissue is from e.g. colon, breast, small intestine, uterine cervix, prostate etc., (many more specified).

Preferred Process; L is detected using specific antibodies and step (c) is by fluorescence-activated cell sorting (FACS). In method (1), the DNA modification is a chemical change; crosslink; mutation; base deletion or insertion, or intercalation, and it may be correlated with a risk factor (exposure to carcinogens, DNA repair defect, oxidative damage or mutation risk). In method (4), L is administered first, followed by at least one isotopically labeled DNA synthesis precursor (P); the two cell populations separated and the SC fraction analyzed to determine isotopic enrichment of one or more deoxyribonucleotides (X) to determine the proliferation ratio. Particularly hydrolysis products of (X) are measured, optionally after chemical modification. Isotope enrichment is determined by mass spectrometry (most preferred), liquid scintillation counting, gamma-counting or NMR, and the method may include calculating the clonal expansion factor of the SC population or the clonal/replicative exhaustion. The preferred P is tritium-labeled dT or **deuterium** -labeled water or **glucose.** In method (5), any change in the proliferation rate caused by administering a test compound indicates that this compound is a therapeutic agent. Preferred test materials are chemicals, dietary factors (e.g. compounds from soya or Brassica, or antioxidants, e.g. genistein, lunasin or Vitamins C, E or A). Method (6) comprises applying method (5) to tissues/individuals who have been treated or not treated with a test compound and comparing the results. Especially

the test compound is a putative lymphocyte co-stimulator and the test material contains such cells.
Preferred Kit: This comprises L and instructions, optionally also an instrument for separation of the SC fraction and a device for administering L. When intended for determining proliferation, it also includes P.

L125 ANSWER 60 OF 76 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-068955 [07] WPIX
DOC. NO. CPI: C2004-028484 [07]
DOC. NO. NON-CPI: N2004-055447 [07]
TITLE: Preparation of tracer composition for measuring metabolic flux in sample, involves the use of 13C metabolite precursor and deuterium source
DERWENT CLASS: B04; K08; S01; S03; S05
INVENTOR: JONES J G; MALLOY C R; SHERRY A D
PATENT ASSIGNEE: (JONE-I) JONES J G; (MALL-I) MALLOY C R; (SHER-I) SHERRY A D
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20030148533	A1	20030807	(200407)*	EN	16[7]	G01N033-48

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20030148533	A1	US 2001-846727	20010501

PRIORITY APPLN. INFO: US 2001-846727 20010501
INT. PATENT CLASSIF.:
MAIN: G01N033-48
BASIC ABSTRACT:
US 20030148533 A1 UPAB: 20050528
NOVELTY - A tracer composition is prepared by obtaining 13C labeled Krebs cycle metabolite precursor that will produce an analyte, and obtaining a deuterium source. Gluconeogenesis is measured from a subject that was provided with the precursor and the deuterium source, and the analyte is produced by comparison of the relative nuclear magnetic resonance profiles of the labeled components in the analyte.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a reagent kit for effecting a simultaneous assay for gluconeogenesis in a sample, comprising a 13C labeled Krebs cycle precursor, and a labeled water tracer.
USE - For the preparation of tracer composition used in the measurement of metabolic flux (related to obesity, diabetes, HIV infection, or other disease conditions as well as physiological events such as exercise, and the effects of drugs) in a sample, e.g. blood, urine or tissue extracts (claimed).
ADVANTAGE - The invention provides a comprehensive analysis of metabolic function.
DESCRIPTION OF DRAWINGS - The figure shows nuclear magnetic resonance spectra consistent with the invention. MANUAL CODE: CPI: B05-A04; B10-A07; B11-C08A; B12-K04E; K08-X; K09-B;
K09-E
EPI: S01-E02A2; S03-E07A; S03-E09X; S03-E14H; S05-D02B3
TECH
ORGANIC CHEMISTRY - Preferred Components: The precursor is glucose,

lactose, lactate or alanine. The analyte is 13C glucose with the label at the 2 and/or 5 positions; **glucose deuterated** in the 2,5 and 6 positions, and any transformation that maintains the 2,5 and 6 positions in relation to one another; pyruvic acid, acetic acid, citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, maleic acid, and/or oxaloacetic acid. 13C3 propionate can also be included. The Krebs cycle precursor is pyruvic acid, acetic acid, acetoacetic acid, beta-hydroxybutyric acid, and/or a Krebs cycle pathway metabolite.

INORGANIC CHEMISTRY - Preferred Component: The deuterium source is deuterated water.

L125 ANSWER 61 OF 76 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1995-283093 [37] WPIX
DOC. NO. CPI: C1995-127740 [37]
TITLE: Detecting lactate produced from labelled glucose - with deuterium and 13C substitutions, used to measure the pentose phosphate pathway in in vitro or in vivo systems
DERWENT CLASS: B04; D16
INVENTOR: KINGSLEY P B; ROSS B D
PATENT ASSIGNEE: (UNMI-C) UNIV MICHIGAN
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 5439803	A	19950808	(199537)*	EN	18[4]	C12P019-02

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5439803	A CIP of	US 1993-106172	19930813
US 5439803	A	US 1993-124514	19930920

PRIORITY APPLN. INFO: US 1993-124514 19930920
US 1993-106172 19930813
INT. PATENT CLASSIF.:
IPC RECLASSIF.: C12P0007-40 [I,C]; C12P0007-56 [I,A]; C12Q0001-54 [I,A]; C12Q0001-54 [I,C]

BASIC ABSTRACT:

US 5439803 A UPAB: 20050702

Labelled lactate (A), produced from glucose by an enzymatic system, is assayed by (i) admin. of D-(1,6-13C2,6,6-2H2) glucose (I) to a system; and (ii) detecting (A) produced from (I).

USE - The method is used to quantify pentose phosphate pathway (PPP) activity in an enzyme system, partic. in a cell culture, cell or tissue sample, or in a living organism (claimed) especially to measure relative amts. of glycolysis and PPP. When combined with microdialysis, the method can be used to monitor glycolysis and PPP (an important pathway for protecting cells against oxidative stress) in vivo, e.g. for screening antioxidant enzyme inhibitors and/or monitoring treatment (e.g. oxidation therapy of cancer).

ADVANTAGE - Double 13C substitution will generate, in a single incubation, labelled lactate methyl gp. derived from both 1 and 6 positions that can be differentiated by gas chromatography-mass spectrometry (GC-MS). This method avoids 14CO2 production (as in the standard method using 1-14C-glucose and 6-14C-glucose), allows repeat measurements to be done on the same set of cells, only involves one incubation and does not require measurement of glucose consumed.

MANUAL CODE: CPI: B05-A04; B10-A07; B10-C04D; B11-C07B5; B12-K04A;

D05-A02; D05-H08; D05-H09

L125 ANSWER 62 OF 76 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1991-273389 [37] WPIX
DOC. NO. CPI: C1991-118573 [21]
DOC. NO. NON-CPI: N1991-208700 [21]
TITLE: Forming image of organs and tissues in vivo - using magnetic resonance imaging after administering deuterium to subject
DERWENT CLASS: B04; K08; P31
INVENTOR: ACKERMAN J J H
PATENT ASSIGNEE: (UNIW-C) UNIV WASHINGTON
COUNTRY COUNT: 1

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 5042488	A	19910827	(199137)*	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5042488	A	US 1986-824203	19860130
US 5042488	A	US 1987-102544	19870929
US 5042488	A	US 1989-391939	19890807

PRIORITY APPLN. INFO: US 1989-391939 19890807
INT. PATENT CLASSIF.:
IPC RECLASSIF.: G01R0033-28 [N,A]; G01R0033-28 [N,C]; G01R0033-44 [I,C]; G01R0033-465 [I,A]
BASIC ABSTRACT:

US 5042488 A UPAB: 20050502

Direct observable deuterium magnetic resonance images of body organs or tissues in vivo and in situ are obtd. using magnetic resonance imaging techniques after administering an appropriate amount of deuterium to the subject.

Deuterium is pref. administered in the form of a deuterated or D-labelled cpd. or cpds., partic. D2O and/or HOD, or **glucose deuterated** at the C-1 position.

USE/ADVANTAGE - Partic. for obtaining images of blood flow, tissue perfusion, brain and heart, avoids the complications of using radio-labelled cpds., and may be able to show up structures not shown by radiography or CT, and structures smaller than those detectable by CT. @(10pp Dwg.No.0/4)

MANUAL CODE: CPI: B04-B04A3; B04-B04D5; B05-C08; B11-C07B5; B12-K04B; K09-B; K09-E

L125 ANSWER 63 OF 76 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 1988-265567 [38] WPIX
DOC. NO. CPI: C1988-118179 [21]
TITLE: New anticancer deuterated aldehyde(s) and their derivs. - prepared from aryl acid halide and deuterium gas in deuterated solvent
DERWENT CLASS: B05
INVENTOR: BORRETSZEN B; BORRETZEN B; DORNISH J M; LARSE R O; LARSEN R O; OFTEBRO R; PETTERSEN E O
PATENT ASSIGNEE: (NHYD-C) NORSK HYDRO AS
COUNTRY COUNT: 18

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 283139	A	19880921	(198838)*	EN	21[0]	
AU 8812331	A	19880915	(198845)	EN		
NO 8800964	A	19881003	(198845)	NO		
JP 63250341	A	19881018	(198847)	JA		
DK 8801297	A	19880912	(198848)	DA		
US 4874780	A	19891017	(198951)#	EN	9	A61K031-335
NO 9201423	A	19880912	(199232)	NO		C07C043-307
US 5149820	A	19920922	(199241)	EN	9[0]	C07D263-04
EP 283139	B1	19930113	(199302)	EN	33[0]	C07B059-00
NO 171631	B	19930104	(199306)	NO		C07B059-00
DE 3877386	G	19930225	(199309)	DE		C07B059-00
NO 172042	B	19930222	(199313)	NO		C07C043-307
ES 2043807	T3	19940101	(199405)	ES		C07B059-00
CA 1327038	C	19940215	(199412)	EN		C07D407-04
JP 2769492	B2	19980625	(199830)	JA	12	C07C047-546
DK 173244	B	20000522	(200032)	DA		C07B059-00

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 283139	A	EP 1988-301440	19880219
US 4874780	A	US 1987-24783	19870311
US 5149820	A Div Ex	US 1987-24783	19870311
DE 3877386	G	DE 1988-3877386	19880219
EP 283139	B1	EP 1988-301440	19880219
DE 3877386	G	EP 1988-301440	19880219
ES 2043807	T3	EP 1988-301440	19880219
NO 9201423	A Div Ex	NO 1988-964	19880304
NO 171631	B	NO 1988-964	19880304
NO 172042	B Div Ex	NO 1988-964	19880304
CA 1327038	C	CA 1988-561032	19880310
DK 173244	B	DK 1988-1297	19880310
JP 63250341	A	JP 1988-56496	19880311
JP 2769492	B2	JP 1988-56496	19880311
US 5149820	A	US 1989-396218	19890821
NO 9201423	A	NO 1992-1423	19920410
NO 172042	B	NO 1992-1423	19920410

FILING DETAILS:

PATENT NO	KIND	PATENT NO
DK 173244 B	Previous Publ	DK 8801297 A
DE 3877386 G	Based on	EP 283139 A
ES 2043807 T3	Based on	EP 283139 A
JP 2769492 B2	Previous Publ	JP 63250341 A
NO 171631 B	Previous Publ	NO 8800964 A
NO 172042 B	Previous Publ	NO 9201423 A
US 5149820 A	Div ex	US 4874780 A

PRIORITY APPLN. INFO: GB 1987-5780 19870311
US 1987-24783 19870311

INT. PATENT CLASSIF.:

MAIN: C07B059-00

IPC RECLASSIF.: A61K0031-075 [I,A]; A61K0031-075 [I,C]; A61K0031-095

[I,A]; A61K0031-095 [I,C]; A61K0031-10 [I,A]; A61K0031-11 [I,A]; A61K0031-11 [I,C]; A61K0031-135 [I,A]; A61K0031-135 [I,C]; A61K0031-335 [I,A]; A61K0031-335 [I,C]; A61K0031-34 [I,A]; A61K0031-34 [I,C]; A61K0031-341 [I,A]; A61K0031-341 [I,C]; A61K0031-385 [I,A]; A61K0031-385 [I,C]; A61K0031-39 [I,A]; A61K0031-39 [I,C]; A61K0031-42 [I,A]; A61K0031-42 [I,C]; A61K0031-421 [I,A]; A61K0031-421 [I,C]; A61K0031-70 [I,A]; A61K0031-70 [I,C]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; C07B0059-00 [I,A]; C07B0059-00 [I,C]; C07C0001-00 [I,A]; C07C0001-00 [I,C]; C07C0013-00 [I,C]; C07C0013-02 [I,A]; C07C0015-00 [I,C]; C07C0015-02 [I,A]; C07C0015-06 [I,A]; C07C0015-073 [I,A]; C07C0201-00 [I,A]; C07C0201-00 [I,C]; C07C0205-00 [I,C]; C07C0205-45 [I,A]; C07C0211-00 [I,C]; C07C0211-27 [I,A]; C07C0223-00 [I,C]; C07C0223-06 [I,A]; C07C0313-00 [I,A]; C07C0313-00 [I,C]; C07C0321-00 [I,C]; C07C0321-20 [I,A]; C07C0321-24 [I,A]; C07C0323-00 [I,C]; C07C0323-16 [I,A]; C07C0323-28 [I,A]; C07C0041-00 [I,A]; C07C0041-00 [I,C]; C07C0043-00 [I,C]; C07C0043-00 [I,C]; C07C0043-164 [I,A]; C07C0043-205 [I,A]; C07C0043-307 [I,A]; C07C0043-307 [I,A]; C07C0045-00 [I,A]; C07C0045-00 [I,C]; C07C0045-41 [I,A]; C07C0047-00 [I,A]; C07C0047-00 [I,C]; C07C0047-52 [I,C]; C07C0047-54 [I,A]; C07C0047-542 [I,A]; C07C0047-546 [I,A]; C07C0047-55 [I,A]; C07C0067-00 [I,A]; C07C0067-00 [I,C]; C07D0263-00 [I,C]; C07D0263-04 [I,A]; C07D0307-00 [I,C]; C07D0307-00 [I,C]; C07D0307-62 [I,A]; C07D0307-62 [I,A]; C07D0407-00 [I,C]; C07D0407-04 [I,A]

SECONDARY: C07H015-04 [I,C]; C07H0009-00 [I,C]; C07H0009-04 [I,A]

BASIC ABSTRACT:

EP 283139 A UPAB: 20050429

Deuterated cpds. of the formula (I) and (II) and their salts are new. In (I), Ar is phenyl substd. by 1-5C alkyl, 3-6C cycloalkyl, halogen, NO2, NH2 or mono- or di-(1-5C alkyl)amino, and Ar is non-deuterated or partly or completely deuterated. In (II) Ar is as defined above and may also be optionally deuterated phenyl; X1 and X2 are each a sulphur, oxygen or nitrogen atom which has attached to it H, 1-5C alkyl, 3-6C cycloalkyl or phenyl or X1 and X2 and the C atom to which they are attached form a cyclic acetal, thioacetal, thiane or oxazolidine; D is a deuterium atom.

Deutero 4,6-O-benzylidene-D-**glucose**; and **deutero** 5,6-O-benzylidene ascorbic acid are specifically claimed.

(I) are prepared by reduction of a cpd. of the formula Ar-CO-X where X is a halogen, with deuterium gas in a solvent in which at least 90% of the protons in the solvent molecules have been replaced by deuterium atoms. Reaction is pref. carried out in the presence of a transition metal catalyst. Pref. solvents are highly deuterated benzene, toluene,, ethyl benzene and xylene. A pure product may be obtained by complexing the aldehyde with NaDSO3 in heavy water.

USE - (I) and (II) are anticancer agents. Pref. they are completely deuterated. Dosages are suitably in the range 0.5-1.5g/sq.m. (I) and (II) may also be used as analgesic agents. Compsns. containing the active cpds. are conventional. They may contain cyclodextrin stabilisers. MANUAL CODE: CPI: B03-F; B07-H; B10-A07; B10-A23; B10-B01A; B10-B01B; B10-B03B; B10-B04A; B10-D01; B12-G07

Member(0006)

ABEQ US 4874780 A UPAB 20050429

A cpd. (I) is claimed where Ar = unsubstd. phenyl or phenyl substd. by 1-5C alkyl, 3-6C cycloalkyl, halogen, NO2, NH2, 1-5C monoalkylamino, 1-5C dialkylamino referring to each alkyl gp., the Ar gp. being non-deuterated

or partly or completely deuterated and X1 and X2 together with the C atom to which they are attached form a cyclic acetal, or a pharmaceutically acceptable salt. Cpd. (I) is pref. deutero 5,6-O-benzylidene ascorbic acid esp. **deutero** 4-6-O-benzylidene-di-**glucose**.

USE/ADVANTAGE - A pharmaceutical compsn. for treating patients with cancer consists essentially of a therapeutically effective amt. of (I) and an pharmaceutically acceptable carrier. (I) shows greater biological activity and: (a) administering high doses frequently; and (b) treatment of patients continuously for several months, and in some cases for years, is reduced. - (9pp)

Member(0008)
ABEQ US 5149820 A UPAB 20050429

Arylheterocyclic cpds. of formula ArCX1X2D (I) and their salts are new. In (I),, Ar = phenyl (opt. substd. by 1-5C alkyl, 3-6C cycloalkyl,halo, NO2, NH2 or mono- or di (1-5C alkyl)amino and opt. wholly or partly deuterated). CX1X2 = a cyclic thioacetal, dithiane or oxazolidine gp. When Ar = phenyl, X1+X2 is not dithiane.

USE - As anticancer agents.

Member(0015)
ABEQ JP 2769492 B2 UPAB 20050429

Deuterated cpds. of the formula (I) and (II) and their salts are new. In (I), Ar is phenyl substd. by 1-5C alkyl, 3-6C cycloalkyl, halogen, NO2, NH2 or mono- or di-(1-5C alkyl)amino, and Ar is non-deuterated or partly or completely deuterated. In (II) Ar is as defined above and may also be optionally deuterated phenyl; X1 and X2 are each a sulphur, oxygen or nitrogen atom which has attached to it H, 1-5C alkyl, 3-6C cycloalkyl or phenyl or X1 and X2 and the C atom to which they are attached form a cyclic acetal, thioacetal, thiane or oxazolidine; D is a deuterium atom.

Deutero 4,6-O-benzylidene-D-**glucose**; and
deutero 5,6-O-benzylidene ascorbic acid are specifically claimed.
(I) are prepd. by reduction of a cpd. of the formula Ar-CO-X where X is a halogen, with deuteruim gas in a solvent in which at least 90% of the protons in the solvent molecules have been replaced by deuterium atoms. Reaction is pref. carried out in the presence of a transition metal catalyst. Pref. solvents are highly deuterated benzene, toluene,, ethyl benzene and xylene. A pure product may be obtained by complexing the aldehyde with NaDSO3 in heavy water.

USE - (I) and (II) are anticancer agents. Pref. they are completely deuterated. Dosages are suitably in the range 0.5-1.5g/sq.m. (I) and (II) may also be used as analgesic agents. Compsns. contg. the active cpds. are conventional. They may contain cyclodextrin stabilisers.

L125 ANSWER 64 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:884408 HCAPLUS Full-text
DOCUMENT NUMBER: 145:244403
TITLE: Process, composition and kit for providing a stable whole blood calibrator/control for glucose determination
INVENTOR(S): Ryan, Wayne L.
PATENT ASSIGNEE(S): Streck, Inc., USA
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006091918	A2	20060831	WO 2006-US6787	20060223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006211072	A1	20060921	US 2006-362362	20060223
PRIORITY APPLN. INFO.:			US 2005-656154P	P 20050223

ED Entered STN: 31 Aug 2006

AB The present invention is directed toward a stable calibrator and/or control, kit and process for using in a glucose monitoring instrumentation. Principally, the instant invention teaches a glycolyzed red blood cell component which has been treated with a glycolysis stabilizing effective amount of at least one non- cross linking aldehyde compound which may be added to fresh plasma along with an amount of glucose to form a simulated whole blood glucose control product, effective for maintaining a particular and essentially stable glucose concentration over a period of time sufficient for accurate measurement and calibration of a glucose measuring instrument.

L125 ANSWER 65 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1218589 HCAPLUS Full-text

DOCUMENT NUMBER: 143:472623

TITLE: Treating human inflammatory and proliferative diseases with fatty acid metabolic inhibitors and glycolytic inhibitors and UCP and FAS antibodies

INVENTOR(S): Newell, Karen Rogers M.

PATENT ASSIGNEE(S): The Regents of the University of Colorado, USA

SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005107801	A2	20051117	WO 2005-US15032	20050428
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,				

MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2004-566746P P 20040429
OTHER SOURCE(S): MARPAT 143:472623
ED Entered STN: 17 Nov 2005
AB The present invention generally relates to systems and methods for treating inflammatory and proliferative diseases, and wounds, using a combination of (1) fatty acid metabolism inhibitors and (2) glycolytic inhibitors and/or UCP and/or Fas inhibitors or antibodies. More particularly, the invention combines an oxirane carboxylic acid compound, represented by etomoxir, with a 2-deoxyglucose compound, represented by 2-deoxy-D-glucose, and/or an antibody against UCP and/or Fas antigen. The systems and methods of the invention can be used to treat drug-resistant or multi-drug resistant cancers (i.e., cancers resistant to conventional cancer drug therapies).

L125 ANSWER 66 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:657023 HCAPLUS Full-text
DOCUMENT NUMBER: 139:176361
TITLE: Anti-glycolytic composition
INVENTOR(S): Le Roux, Carel Wynand; Wilkinson, Stephen P.; Muller, Bruce Ronald; Alaghband-Zadeh, Jamshid; Pavitt, Darrell Vincent
PATENT ASSIGNEE(S): IC Innovations Ltd., UK
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003069344	A1	20030821	WO 2003-GB650	20030212
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003208411	A1	20030904	AU 2003-208411	20030212
PRIORITY APPLN. INFO.:			GB 2002-3280 A	20020212
			WO 2003-GB650 W	20030212

ED Entered STN: 22 Aug 2003
AB The present invention provides a composition comprising (i) glyceraldehyde, or a mimetic thereof; (ii) a glycolytic inhibitor; and (iii) an anti-coagulating agent. The invention also relates to the use of said composition to inhibit glycolysis in a tissue sample. Further aspects of the invention relate to an assay for detecting the level of glucose in a tissue sample, and a kit for preserving glucose levels in a tissue sample.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 67 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:173640 HCAPLUS Full-text
DOCUMENT NUMBER: 138:219717
TITLE: Genes that are differentially regulated under hypoxic

conditions and their diagnostic and therapeutic uses
INVENTOR(S): Kingsman, Susan Mary; White, Jonathan; Ward, Neil Raymond; Harris, Robert Alan; Naylor, Stuart; Mundy, Christopher Robert
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK
SOURCE: PCT Int. Appl., 424 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018621	A2	20030306	WO 2002-GB3892	20020823
WO 2003018621	A8	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002313559	A1	20030310	AU 2002-313559	20020823

PRIORITY APPLN. INFO.:

GB 2001-20558	A	20010823
GB 2001-24037	A	20011005
WO 2002-GB3892	W	20020823

ED Entered STN: 07 Mar 2003

AB This invention relates to novel genes and gene products that are implicated in certain disease states. The Smartomics method was utilized to improve the discovery of genes activated or repressed in response to hypoxia in primary human macrophages. This involves augmenting the natural response to hypoxia by exptl. introducing key regulators of the hypoxia response, namely hypoxia-inducible factor 1 (HIF-1) and HIF-2 (also known as EPAS1), into a population of primary human macrophages and comparing gene expression in these cells with that in control cells. The expression of certain polypeptides was induced under conditions of hypoxia, as mimicked by adenoviral overexpression of HIF-1α or EPAS1. The expression of certain of these hypoxia-regulated genes is responsive to cytokines and other mols., including tumor necrosis factor α, interleukin 1β (IL-1β), lipopolysaccharide and γ-interferon, IL-12, IL-15, IL-17, IL-13, IL-4, IL-10, and superoxide. Differential expression is also noted in various cell types and tissues, and in in tumors, chronic obstructive pulmonary disease, and artherosclerosis. Thus, the invention provides for the diagnosis and therapeutic targets for hypoxia-regulated conditions. Also, methods for the detection of mutations or abnormal expression levels of the transcripts and their encoded protein products are provided.

L125 ANSWER 68 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:811862 HCAPLUS Full-text
DOCUMENT NUMBER: 139:288644
TITLE: Methods and compositions for preserving glucose level in blood specimens
INVENTOR(S): Landt, Michael
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: U.S., 14 pp.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6632844	B1	20031014	US 2001-816493		20010323
PRIORITY APPLN. INFO.:			US 2000-192971P	P	20000329

ED Entered STN: 16 Oct 2003
AB The invention relates to methods and compns. for preserving blood samples. In particular, a method for stabilizing glucose level in a blood sample is provided, which method comprises adding an effective amount of glyceraldehyde to a blood sample, whereby glucose level in said blood sample remains substantially constant for a period of time. Kits and combinations for stabilizing glucose level in a blood sample are also provided.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 69 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:814181 HCAPLUS Full-text
DOCUMENT NUMBER: 137:323129
TITLE: A splice variant of the EGLN3 gene product retaining normal biological activity in the hypoxic response and its diagnostic and therapeutic uses
INVENTOR(S): White, Jonathan; Harris, Robert Alan; Kan, On; Mundy, Christopher Robert; Ward, Neil Raymond; Kingsman, Susan Mary; Naylor, Stuart; Rayner, William Nigel; Binley, Katie Mary
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002083728	A2	20021024	WO 2002-GB1662		20020408
WO 2002083728	A3	20030213			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2003203372	A1	20031030	US 2002-170385		20020612
PRIORITY APPLN. INFO.:			GB 2001-9008	A	20010410
			GB 2000-30076	A	20001208
			GB 2001-3156	A	20010208
			GB 2001-25666	A	20011025
			WO 2001-GB5458	A2	20011210
			WO 2002-GB1662	A2	20020408

ED Entered STN: 25 Oct 2002

AB This invention relates to a novel isoform of the EGLN3 gene product that has been implicated in certain disease states. This novel isoform lacks an internal stretch of nucleotides form the wild type gene, probably due to an alternative splicing event. Both the full length EGLN3 protein and EGLN3 splice variant have been shown to be biol. active. Overexpression of both these isoforms reduce HIF-mediated gene expression through HRE reporters, thus demonstrating their role in the HIF signalling pathway. The suppression effect of the EGLN3 splice variant appears to be stronger than that of the full length EGLN3 protein.

L125 ANSWER 70 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:449920 HCAPLUS Full-text
DOCUMENT NUMBER: 137:29000
TITLE: Identification of genes and gene products involved in disease states and specifically in hypoxia by comparison of differentially regulated transcriptome or proteome constituents
INVENTOR(S): White, Jonathan; Mundy, Christopher Robert; Ward, Neil Raymond; Krige, David; Kingsman, Susan Mary; Harris, Robert Alan; Rayner, William Nigel
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Limited, UK
SOURCE: PCT Int. Appl., 538 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002046465	A2	20020613	WO 2001-GB5458		20011210
WO 2002046465	A3	20031106			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002020920	A5	20020618	AU 2002-20920		20011210
US 2003203372	A1	20031030	US 2002-170385		20020612
PRIORITY APPLN. INFO.:			GB 2000-30076	A	20001208
			GB 2001-3156	A	20010208
			GB 2001-25666	A	20011025
			GB 2001-9008	A	20010410
			WO 2001-GB5458	W	20011210
			WO 2002-GB1662	A2	20020408

ED Entered STN: 14 Jun 2002
AB This invention relates to novel methods for the identification of genes and gene products that are implicated in certain disease states. According to the invention, there is provided a method for the identification of a gene that is implicated in a specific disease or physiol. condition, said method comprising the steps of comparing: (i) the transcriptome or proteome of a first specialized cell type that is implicated in the disease or condition under first and second exptl. conditions; with (ii) the transcriptome or proteome of a second specialized cell type under said first and said second exptl.

conditions; and identifying as a gene implicated in the disease or physiol. condition, a gene that is differentially regulated in the two specialized cell types under the first and second exptl. conditions. The invention also relates to novel genes and gene products identified using these methods. Thus, expressed 488 mRNAs and their protein products are provided by comparison of the hypoxic response between human macrophages and cardiomyoblasts by a subtraction cloning/array screening approach. These transcripts and proteins have applications in protein or gene therapy, in diagnosis of disease (e.g., hypoxic-related) states, and in screening for agonists and/or antagonists ligands.

L125 ANSWER 71 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:740671 HCAPLUS Full-text
DOCUMENT NUMBER: 138:333838
TITLE: Quantitation of absolute 2H enrichment of plasma glucose by 2H NMR analysis of its monoacetone derivative
AUTHOR(S): Jones, John G.; Perdigoto, Rui; Rodrigues, Tiago B.; Geraldes, Carlos F. G. C.
CORPORATE SOURCE: Department of Biochemistry and Center for Neuroscience and Cell Biology, Faculty of Sciences and Technology, University of Coimbra, Coimbra, Port.
SOURCE: Magnetic Resonance in Medicine (2002), 48(3), 535-539
CODEN: MRMEEN; ISSN: 0740-3194
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 30 Sep 2002
AB A simple 2H NMR method for quantifying absolute 2H-enrichments in all seven aliphatic positions of glucose following its derivatization to monoacetone glucose is presented. The method is based on the addition of a small quantity of 2H-enriched formate to the NMR sample. When the method was applied to [2-2H]monoacetone glucose samples prepared from [2-2H]glucose stds. of known enrichments in the range of 0.2-2.5%, enrichment ests. derived by the NMR method were in good agreement with the real enrichment values of the [2-2H]glucose precursors. The measurement was also applied to monoacetone glucose derived from human plasma glucose samples following administration of 2H2O and attainment of isotopic steady state, where glucose H2 and body water enrichment are equivalent In these studies, the absolute H2 enrichment of plasma glucose estimated by the formate method was in good agreement with the 2H-enrichment of body water measured by an independent method.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 72 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:130432 HCAPLUS Full-text
DOCUMENT NUMBER: 137:168052
TITLE: Modeling **Deuterated Glucose** Labeling of T-lymphocytes
AUTHOR(S): Ribeiro, Ruy M.; Mohri, Hiroshi; Ho, David D.; Perelson, Alan S.
CORPORATE SOURCE: Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM, 87545, USA
SOURCE: Bulletin of Mathematical Biology (2002), 64(2), 385-405
CODEN: BMTBAP; ISSN: 0092-8240
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal

LANGUAGE: English
ED Entered STN: 20 Feb 2002
AB Human immunodeficiency virus type 1 (HIV-1) infects cells of the immune system and leads to depletion of CD4 + T cells, and to an increase of CD8 + T-lymphocytes. However, not much is known about the dynamics of turnover (proliferation and death) of the CD4 + and CD8 + T cell populations in HIV-infected and healthy individuals. A new exptl. technique has been developed using deuterated-glucose labeling that provides information on cell turnover in vivo. However, the quant. interpretation of the data requires the development of specific dynamic models. In this paper we derive two models, a simple one-compartment model and a more complex two-compartment model. These models allow for robust quantification of death and proliferation rates, but careful consideration of the system is necessary to understand what is being measured in each case. We demonstrate that more realistic models can account not only for differences in the turnover rates between HIV-infected and healthy individuals, but also take into consideration the elevated state of activation in HIV infection. The use of these models in the interpretation of the exptl. data will increase our knowledge of T cell dynamics in the context of HIV infection. (c) 2002 Society for Mathematical Biology.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L125 ANSWER 73 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:755306 HCAPLUS Full-text
DOCUMENT NUMBER: 133:278376
TITLE: A method and kit for measuring mitochondrial activity
INVENTOR(S): Bovina, Carla; Lenaz, Giorgio; Tura, Sante; Catani, Lucia; Merlo Pich, Milena
PATENT ASSIGNEE(S): Universita' Degli Studi di Bologna, Italy
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

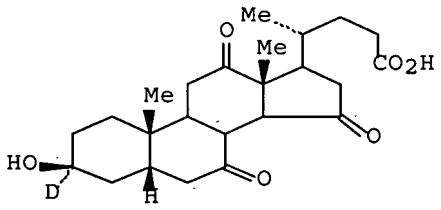
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1046714	A2	20001025	EP 2000-830232	20000328
EP 1046714	A3	20010124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
IT 1310359	B1	20020213	IT 1999-BO185	19990420
US 6261796	B1	20010717	US 2000-550013	20000414
JP 2000333697	A	20001205	JP 2000-118328	20000419
PRIORITY APPLN. INFO.:			IT 1999-BO185 A	19990420

ED Entered STN: 26 Oct 2000
AB The present invention relates to a method for measuring mitochondrial activity by measuring platelet Δ lactate. The present invention also relates to a new method for dosing the quantity of platelet lactate using the chromogenic agent 3-acetylpyridine-NAD+ and the ox heart LDH enzyme. The present invention also relates to a diagnostic (micromethod) kit.

L125 ANSWER 74 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:73997 HCAPLUS Full-text
DOCUMENT NUMBER: 120:73997
TITLE: Generation of L-[2-2H, 2-13C]lactic acid by erythrocytes exposed to D-[2-13C]glucose in the presence of deuterium oxide

AUTHOR(S): Malaisse, W. J.; Willem, R.
CORPORATE SOURCE: Erasmus Med. Sch., Brussels Free Univ., Brussels, Belg.
SOURCE: Medical Science Research (1993), 21(17), 631-2
CODEN: MSCREJ; ISSN: 0269-8951
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 19 Feb 1994
AB A model was proposed for the prevalent generation of NAD2H in erythrocytes exposed to D-glucose in the presence of 2H2O.

L125 ANSWER 75 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:424327 HCAPLUS Full-text
DOCUMENT NUMBER: 113:24327
TITLE: Efficient preparative-scale enzymatic synthesis of specifically deuterated bile acids
AUTHOR(S): Riva, Sergio; Ottolina, Gianluca; Carrea, Giacomo; Danieli, Bruno
CORPORATE SOURCE: Ist. Chim. Ormoni, CNR, Milan, 20131, Italy
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1989), (11), 2073-4
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:24327
ED Entered STN: 21 Jul 1990
GI



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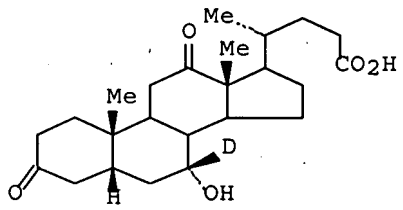

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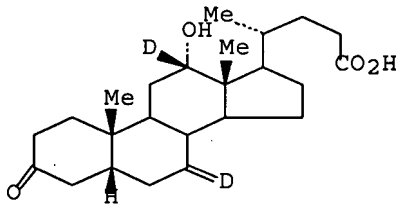

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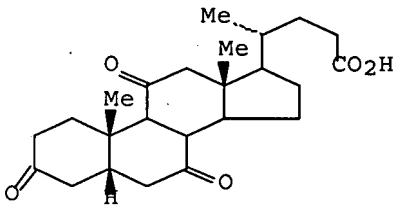

IV

AB The regio- and stereospecific synthesis of deuterated bile acids I, II, and III has been achieved by coupling the reduction of cholanoic acid IV, catalyzed by 3β,17β-hydroxy steroid dehydrogenase, to the oxidation of [1-2H]glucose, catalyzed by glucose dehydrogenase. The transfer of deuterium from glucose to bile acid was mediated by talytic amts. of coenzyme continuously recycled in situ. The isotopic purity of deuteriated bile acids, determined by 1H NMR spectrometry, was ≥94%.

L125 ANSWER 76 OF 76 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1946:37965 HCAPLUS Full-text
DOCUMENT NUMBER: 40:37965
ORIGINAL REFERENCE NO.: 40:7332i,7333a-d
TITLE: Studies in carbohydrate metabolism. VII. The distribution of deuterium in a sample of **deuterio-glucose** excreted by a diabetic rabbit
AUTHOR(S): Stetten, DeWitt, Jr.; Stetten, Marjorie R.
CORPORATE SOURCE: Columbia Univ.
SOURCE: Journal of Biological Chemistry (**1946**), 165, 147-55
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 16 Dec 2001
AB cf. C.A. 40, 2874.1. A pooled urinary glucose sample excreted over a 48-hr. period by a rabbit rendered diabetic with alloxan was analyzed for its percentage of C-bound D concentration on each of the 6 glucose C atoms. The rabbit was consuming ad libitum a diet containing 62% carbohydrate, and its body fluids contained 1.05 to 1.09 atom % excess of D. The urinary glucose was isolated as the pentaacetate, and this product contained 0.159 atom % D, from which the average D concentration in the 7 stable H atoms of glucose was calculated as 0.159 + 22/7 = 0.500 atom % D. Suitable derivs. were prepared from this material so that for each derivative a definite C-bound H was eliminated. Each derivative was analyzed for its D content. The derivs. which were prepared, and the position of the C from which the H was lost (C1 is the aldehyde C) were: K gluconate and glucobenzimidazole for C1; glucosazone for C2; K acid saccharate and Ag saccharate for C1 and C6; 2,3,4,6-tetramethylglucose from the pentaacetate followed by HNO3 oxidation to a mixture of xylotrimethoxyglutaric (I) and d-dimethoxy succinic acids, both isolated as the amides, where the former arose by loss of C6 and the latter by loss of C5 and C6; of the 7 H atoms initially bound to C in glucose, the I still retained those in positions 2, 3, and 4, whereas in the latter compound the H in positions 2 and 3 would only be retained. D was thus demonstrated to be present at each position, and its concentration at each of the several positions was found to be of the same order of magnitude. The only significant deviation from the average value was at position C5 where a somewhat higher D concentration was found than at the other positions. The results rule out reversible enolization of glucose as a major metabolic pathway, and support the view that the concentration of D in a sample of urinary glucose, excreted by an animal receiving D2O, is a measure of the amount of glucose synthesized.